



## **PATIENT SAFETY**

### **October 2004**

1: Acad Emerg Med. 2004 Jul;11(7):766-70.

Profiles in patient safety: when an error occurs.

Hobgood C, Hevia A, Hinchey P.

Department of Emergency Medicine, University of North Carolina School of Medicine, Chapel Hill, NC 27599, USA. hobgood@med.unc.edu

Medical error is now clearly established as one of the most significant problems facing the American health care system. Anecdotal evidence, studies of human cognition, and analysis of high-reliability organizations all predict that despite excellent training, human error is unavoidable. When an error occurs and is recognized, providers have a duty to disclose the error. Yet disclosure of error to patients, families, and hospital colleagues is a difficult and/or threatening process for most physicians. A more thorough understanding of the ethical and social contract between physicians and their patients as well as the professional milieu surrounding an error may improve the likelihood of its disclosure. Key among these is the identification of institutional factors that support disclosure and recognize error as an unavoidable part of the practice of medicine. Using a case-based format, this article focuses on the communication of error with patients, families, and colleagues and grounds error disclosure in the cultural milieu of medical ethics.

Publication Types:

Case Reports

PMID: 15231468 [PubMed - indexed for MEDLINE]

2: Acta Trop. 2004 Jul;91(2):153-60.

Comparison of the effectiveness of two topical paromomycin treatments versus meglumine antimoniate for New World cutaneous leishmaniasis.

Armijos RX, Weigel MM, Calvopina M, Mancheno M, Rodriguez R.

Health Sciences Program, College of Health Sciences, Room 705, 1101 North Campbell Street, The University of Texas at El Paso, El Paso, TX 79902-0581, USA.

The randomized, controlled study compared the therapeutic efficacy and safety of two paromomycin-containing topical preparations with the gold treatment standard, meglumine antimoniate, and with each other in 120 Ecuadorian patients with ulcerated lesions. The two paromomycin treatment comparisons were double-blinded. Group 1 (n = 14) received 15% paromomycin plus 12% methylbenzoniun chloride (PR-MBCL) dissolved in a soft white paraffin base, applied twice daily for 30 days. Group 2 (n = 40) was also treated for 30 days with 15% paromomycin plus 10% urea (PR-U) dissolved in the same paraffin base. Group 3 (n = 40) received 20mg/kg/day of IM meglumine antimoniate (MA) for 10

days as per Ecuadorian Ministry of Public Health recommendations at the time of the study. The 10-day treatment was completed by 90% of the MA group compared to 72.5% of the PR-MBCL ( $X^2 = 4.0$ ,  $P = 0.045$ ) and 75% of the PM-U ( $X^2 = 3.1$ ,  $P > 0.05$ ) groups whose treatment regime lasted 20 days longer than the MA treatment. Post-treatment lesion burning, redness, inflammation, and soreness were more common in the two paromomycin groups compared to MA group ( $P < 0.05$ ). The frequency of treatment-related side effects in the two paromomycin groups was similar. Six weeks after the start of treatment, 80.6% of MA subjects were clinically cured compared to 48.3% in the PR-MBCL ( $X^2 = 6.1$ ,  $P = 0.014$ ) and 40% in the PM-U groups ( $X^2 = 12.6$ ,  $P = 0.002$ ). By 12 weeks, the proportion of clinically cured subjects in the MA (91.7%) compared to PM-MBCL (79.3%) or PM-U (70%) groups was not significantly different ( $P > 0.05$ ). MA-treated subjects clinically cured by 12 weeks had a faster mean healing time (29.5 +/- 12.2 days) compared to those in the PM-MBCL (versus 43.1 +/- 14.4 days,  $t = -3.7$ ,  $P = 0.001$ ) or PR-U groups (43.5 +/- 17 days;  $t = -3.2$ ,  $P = 0.002$ ). During the 48-week post-treatment follow-up period, infection reactivation was observed in 15.2% of the MA subjects compared to 17.4% in the PM-MBCL and 10.5% PM-U of subjects diagnosed as clinically healed by 12 weeks ( $P > 0.05$ ). The results suggest that although the time required for the clinical healing of ulcerated lesions takes longer, topical paromomycin may be an acceptable therapeutic alternative in endemic areas where meglumine antimoniate is not available, is too costly or medically contraindicated.

Publication Types:

Clinical Trial  
Randomized Controlled Trial

PMID: 15234664 [PubMed - indexed for MEDLINE]

3: Addiction. 2004 Jul;99(7):811-28.

Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: a systematic review.

Carmen B, Angeles M, Ana M, Maria AJ.

Agency for Health Technology Assessment, Madrid, Spain. cbouza@iscii.es

AIMS: To ascertain the efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence. METHODS: Systematic review of the literature (1990-2002) and meta-analysis of full published randomized and controlled clinical trials assessing acamprosate or naltrexone therapy in alcohol dependence. Estimates of effect were calculated according to the fixed-effects model. MEASUREMENTS: Relapse and abstinence rates, cumulative abstinence duration and treatment compliance were considered as primary outcomes. Findings Thirty-three studies met the inclusion criteria. Acamprosate was associated with a significant improvement in abstinence rate [odds ratio (OR): 1.88 (1.57, 2.25),  $P < 0.001$ ] and days of cumulative abstinence [WMD: 26.55 (17.56, 36.54)]. Short-term administration of naltrexone reduced the relapse rate significantly [OR: 0.62 (0.52, 0.75),  $P < 0.001$ ], but was not associated with a significant modification in the abstinence rate [OR: 1.26 (0.97, 1.64),  $P = 0.08$ ]. There were insufficient data to ascertain naltrexone's efficacy over more prolonged periods. Acamprosate had a good safety pattern and was associated with a significant improvement in treatment compliance [OR: 1.29 (1.13, 1.47),  $P < 0.001$ ]. Naltrexone's side effects were more numerous, yet the drug was nevertheless tolerated acceptably without being associated with a lower adherence to treatment (OR: 0.94 (0.80, 1.1),  $P = 0.5$ ). However, overall compliance was relatively low with both medications. CONCLUSIONS: Both

acamprosate and naltrexone are effective as adjuvant therapies for alcohol dependence in adults. Acamprosate appears to be especially useful in a therapeutic approach targeted at achieving abstinence, whereas naltrexone seems more indicated in programmes geared to controlled consumption. Both drugs are safe and acceptably tolerated but issues of compliance need to be addressed adequately to assure their usefulness in clinical practice.

Publication Types:

Meta-Analysis  
Review  
Review, Academic

PMID: 15200577 [PubMed - indexed for MEDLINE]

4: Alcohol Alcohol. 2004 Jul-Aug;39(4):271-5.

Challenges to medications development in treating alcohol dependence: an international perspective.

Littleton JM, De Witte P, Litten R, Gessa GL, Spanagel R, Kranzler H, Lehert P, Johnson B, Saunders J, Berglund M, Harris A, Anton R, Mann K.

Department of Molecular and Biomedical Pharmacology, University of Kentucky, Cooper and University Drives, Lexington 40546-0236, USA. jlittle@uky.edu

Few medications for treating alcohol dependence exist. Greater partnership is needed between academia and the pharmaceutical industry to develop, licence and market efficacious medications for treating alcohol dependence. Methodologies that span the divide between preclinical and large-scale clinical studies need to be developed in order to provide sufficient information on safety, toleration, drug-interaction profile and efficacy, with which to guide development decisions. Due to the heterogeneous nature of alcohol dependence, the effort of developing an efficacious medication is likely to be enhanced by clearer choices about the characteristics of the population. Careful consideration of potential mechanism of action of the putative therapeutic medication should enable the appropriate choice of drinking endpoint. The pharmaceutical industry in collaboration with academia might need to develop new approaches to determining appropriate treatment endpoints with regulatory bodies. The investment risk to industry should be appraised not only in terms of the rather poor results of previous marketing efforts but with a view to the opportunity to penetrate a potentially enormous and largely untapped market.

Publication Types:

Congresses

PMID: 15208155 [PubMed - indexed for MEDLINE]

5: Am Heart J. 2004 Jul;148(1):e4.

Efficacy and safety of rosuvastatin and atorvastatin in patients with hypercholesterolemia and a high risk of coronary heart disease: a randomized, controlled trial.

Schwartz GG, Bolognese MA, Tremblay BP, Caplan R, Hutchinson H, Raza A, Cressman M.

University of Colorado, Denver VA Medical Center, Denver, Colo 80220, USA.

Gregory.Schwartz@med.va.gov

BACKGROUND: This double-blind, multicenter, randomized trial compared rosuvastatin and atorvastatin for reducing low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia and a high risk of coronary heart disease. METHODS: After a 6-week dietary lead-in period, patients with LDL-C levels > or =160 and <250 mg/dL and triglyceride levels < or =400 mg/dL were

randomly assigned to 24 weeks' treatment in 1 of 3 groups, each with forced dose titrations at 12 and 18 weeks. Starting and titrated doses for each group were rosuvastatin 5, 20, and 80 mg (n = 127); rosuvastatin 10, 40, and 80 mg (n = 128); and atorvastatin 10, 40, and 80 mg (n = 128). RESULTS: At 24 weeks, LDL-C was reduced significantly more with 80 mg rosuvastatin (combined rosuvastatin group) than with atorvastatin 80 mg (60% vs 52% [P <.001]). At 12 weeks, rosuvastatin 5 and 10 mg reduced LDL-C significantly more than atorvastatin 10 mg (40% [P <.01], 47% [P <.001] vs 35%). At 18 weeks, LDL-C reductions were also significantly greater in both rosuvastatin groups than in the atorvastatin group (52% [P <.01], 59% [P <.001] vs 47%). Consequently, more patients receiving rosuvastatin achieved LDL-C goals. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), non-HDL-C, apolipoproteins B and A-I, and all lipid ratios were more favorably modified by rosuvastatin at 24 weeks (P <.01). Effects of the 2 agents on triglycerides were similar. CONCLUSIONS: Rosuvastatin was more efficacious than atorvastatin in modifying lipids in patients with hypercholesterolemia and a high coronary heart disease risk.

Publication Types:

Clinical Trial  
Multicenter Study  
Randomized Controlled Trial

PMID: 15215813 [PubMed - indexed for MEDLINE]

6: Am J Respir Crit Care Med. 2004 Aug 15;170(4):445-9. Epub 2004 Jun 01. Treatment completion and costs of a randomized trial of rifampin for 4 months versus isoniazid for 9 months.

Menzies D, Dion MJ, Rabinovitch B, Mannix S, Brassard P, Schwartzman K. Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, 3650 St-Urbain, Room K1.24, Montreal, PQ, H2X 2P4 Canada. dick.menzies@mcgill.ca

There is little published information regarding treatment completion, safety, and efficacy of rifampin administered daily for 4 months—a recommended alternative to 9 months of isoniazid for therapy of latent tuberculosis infection. In an open-label randomized trial at a university-affiliated respiratory hospital, consenting patients whose treating physician had recommended therapy for latent tuberculosis infection were randomized to daily self-administered rifampin for 4 months or daily self-administered isoniazid for 9 months. Of 58 patients randomized to rifampin, 53 (91%) took 80% of doses, and 50 (86%) took more than 90% of doses within 20 weeks compared with 44 (76%) and

36 (62%) who took 80 and 90%, respectively, of doses of isoniazid within 43 weeks (relative risks: 80% of doses, 1.2 [95% confidence interval: 1.02, 1.4]; 90% of doses, 1.4 [1.1, 1.7]). Adverse events resulted in permanent discontinuation of therapy for two (3%) patients taking rifampin, and for eight (14%) patients taking isoniazid. Three patients developed drug-induced hepatitis—all were taking isoniazid. Total costs of therapy were significantly higher for isoniazid. In conclusion, completion of therapy was significantly better with 4 months of rifampin and major side effects were somewhat lower. Further studies are needed to assess the safety and efficacy of the 4-month rifampin regimen.

Publication Types:

Clinical Trial  
Randomized Controlled Trial

PMID: 15172892 [PubMed - indexed for MEDLINE]

7: Ann Pharmacother. 2004 Jul-Aug;38(7-8):1323-4; author reply 1324. Epub 2004 Jun 08.

Comment on:

Ann Pharmacother. 2003 Nov;37(11):1712-5.

Comment: safety and efficacy of influenza vaccine in children.

van der Wouden JC, Bueving HJ.

Publication Types:

Comment

Letter

PMID: 15187221 [PubMed - indexed for MEDLINE]

8: Ann Pharmacother. 2004 Jul-Aug;38(7-8):1236-42. Epub 2004 Jun 08.

Omalizumab: a novel therapy for allergic asthma.

Davis LA.

Department of Pharmacy, University of Virginia Health System, PO Box 800674, Charlottesville, VA 22908-0674, USA. Id4z@virginia.edu

OBJECTIVE: To review the pharmacology, efficacy, and safety of omalizumab, focusing on the treatment of allergic asthma. DATA SOURCES: A MEDLINE search (1966-November 2003) was conducted using the key words omalizumab, Xolair, and Rhu-MAB25, with studies limited to those in humans and published in English. References of identified articles were reviewed for additional citations. STUDY

SELECTION AND DATA EXTRACTION: Clinical trials evaluating the pharmacology, efficacy, and safety of omalizumab for treatment of allergic asthma in patients aged  $\geq 12$  years were selected. Clinical trials examining utility in pediatric patients were also reviewed. DATA SYNTHESIS: Omalizumab's ability to form complexes with unbound immunoglobulin E (IgE) translates into decreased unbound serum IgE levels and high-affinity IgE receptors on basophils, as well as attenuation of early and late allergic response in patients with allergic asthma. Results of clinical trials demonstrated that omalizumab administered subcutaneously is a safe and effective treatment for moderate to severe allergic asthma. Generally, omalizumab has a mild adverse effect profile. Omalizumab may be particularly useful for treatment of moderate to severe allergic asthma in patients who are poorly controlled on conventional therapy, experience adverse effects secondary to high-dose or prolonged corticosteroid treatment, or who have frequent exacerbations because of poor medication adherence. The high cost associated with omalizumab treatment may be prohibitive for some patients, thereby limiting its utility. CONCLUSIONS: Omalizumab is a safe and effective therapy for treatment of moderate to severe allergic asthma in difficult-to-treat, high-risk patients.

Publication Types:

Review

Review, Tutorial

PMID: 15187202 [PubMed - indexed for MEDLINE]

9: Ann Pharmacother. 2004 Jul-Aug;38(7-8):1130-5. Epub 2004 Jun 01.

Comparing dexmedetomidine prescribing patterns and safety in the naturalistic setting versus published data.

Dasta JF, Kane-Gill SL, Durtschi AJ.

College of Pharmacy, The Ohio State University, Columbus, OH 43210-1291, USA.

Dasta.1@osu.edu

**BACKGROUND:** In clinical practice, new drugs may be used differently than the product labeling recommends. Furthermore, it often takes several years of use before adverse drug reactions (ADRs) are reported. **OBJECTIVE:** To compare prescribing patterns and safety of the newly released drug dexmedetomidine as observed in clinical practice with published data on the drug. **METHODS:** Information from a convenience sample of adults receiving dexmedetomidine as part of routine patient care at 10 institutions was retrospectively collected from June 27, 2001, to May 31, 2002. Investigators reviewed medical records daily and entered dosing information, patient demographics, and predefined categories of ADR severity and probability anonymously via the Internet on a secure server. **RESULTS:** Only 33% of the total sample (n = 136) of patients received a loading infusion of dexmedetomidine; however, maintenance dosing was usually within product labeling guidelines. Of note, 27.2% of patients received dexmedetomidine above the maximum dose and 33.8% received the drug beyond 24 hours. Some patients (15.4%) were never mechanically ventilated, while 59.5% received dexmedetomidine following extubation for an average of 11.3 hours. ADRs were reported in 30% of patients: 20% of the reactions required treatment or increased length of stay. Hypotension was the most common ADR, occurring in 22.7% of patients. Bradycardia was reported in 4.4% of patients. The rate and type of ADRs were similar in patients receiving dexmedetomidine >24 hours compared with the total population. **CONCLUSIONS:** Dexmedetomidine is prescribed within product labeling guidelines except for low use of a loading dose, some patients received the drug at doses above the maximum, and others received it for longer than 24 hours. Since ADR rates are similar to those of other published reports, dexmedetomidine maintained its expected safety profile in our patients.

PMID: 15173557 [PubMed - indexed for MEDLINE]

10: Ann Pharmacother. 2004 Jul-Aug; 38(7-8):1272-7. Epub 2004 Jun 01.  
Etomidate for procedural sedation in the emergency department.

Falk J, Zed PJ.

Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, Canada.

**OBJECTIVE:** To review the current efficacy and safety evidence for the use of etomidate for procedural sedation in the emergency department (ED). **DATA SOURCES:** MEDLINE (1966-December 2003), EMBASE (1980-December 2003), PubMed (1966-December 2003), and Cochrane Database of Systemic Reviews (up to December 2003) were searched for full-text reports published in English on the use of etomidate in humans. Search terms included etomidate, procedural sedation, conscious sedation, relocation, dislocation, abscess incision, abscess drainage, and cardioversion. **STUDY SELECTION AND DATA EXTRACTION:** Prospective and retrospective studies evaluating efficacy or safety endpoints using etomidate for procedural sedation in the ED were included. All studies were evaluated independently by both authors. For clinical outcomes (efficacy, safety), the definitions specified by each study were used. **DATA SYNTHESIS:** Three observational studies and 5 prospective, randomized controlled trials were included in this review. Onset of action and time to recovery following etomidate were rapid and found to be comparable to that of propofol and thiopental but significantly faster than that of midazolam. The dose of etomidate for procedural sedation ranged from 0.15 to 0.22 mg/kg. No significant hemodynamic effects were observed; however, respiratory depression resulting in

oxygen desaturation to <90% or apnea appears to occur in approximately 10% of patients undergoing procedural sedation with etomidate with or without analgesia. The most prominent adverse effect reported with etomidate was myoclonus, occurring in 20-45% of patients. CONCLUSIONS: Etomidate is an appropriate and valuable agent for performing procedural sedation in the ED. The rapid onset and recovery time and relative lack of significant hemodynamic and respiratory effects may facilitate optimal and safe conditions for procedural sedation in the ED.

Publication Types:

Review

Review, Tutorial

PMID: 15173551 [PubMed - indexed for MEDLINE]

11: Ann R Coll Surg Engl. 2004 Jul;86(4):260-2.

A safe, simple and cost-effective protocol for blood transfusion in primary total knee replacement.

Mehra A, Murray J, deAlwis C.

Orthopaedic and Haematology Department, Royal Glamorgan Hospital, Ynysmaerdy, Llantrisant CF72 8XR, South Wales, UK.

BACKGROUND: Patients undergoing total knee replacement (TKR) in the UK usually have either blood cross-matched or have an auto-transfusion of drained blood postoperatively. A previous retrospective audit of blood requirements in patients who had undergone primary TKR showed that a large amount of cross-matched blood was wasted as the CT ratio (ratio of number of units of blood cross-matched to number of units transfused) of 4.9:1 was obtained. The range recommended by the Blood Transfusion Society is 2:1 to 3:1. METHODS: A protocol was introduced to group and save plus antibody screen for all patients and to cross-match 2 units of blood pre-operatively in patients with either a haemoglobin of less than 12.5 g/dl or with multiple red cell antibodies in their blood. The trigger point for blood transfusion postoperatively was also reduced from 9.0 g/dl to 8.0 g/dl, unless the patient was clinically symptomatic.

RESULTS: A further prospective study involving 50 patients was carried out using the new protocol. Five patients required cross-matching pre-operatively, three with haemoglobin less than 12.5 g/dl and two with multiple red cell antibodies. Postoperatively, the patients with haemoglobin of less than 12.5 g/dl required blood transfusion of 2 units each, reducing the CT ratio to 1.7:1. The patients with red cell antibodies did not require a blood transfusion. CONCLUSIONS: The benefits from above protocol are 2-fold: patient safety, as risks of transfusion are avoided; and cost saving, in regards to haematology technician time and auto-transfusion sets which cost around pound 70 each.

PMID: 15239867 [PubMed - indexed for MEDLINE]

12: Arch Intern Med. 2004 Jul 12;164(13):1395-404.

Efficacy of pharmacotherapy for weight loss in adults with type 2 diabetes mellitus: a meta-analysis.

Norris SL, Zhang X, Avenell A, Gregg E, Schmid CH, Kim C, Lau J.

Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA 30341, USA. scn5@cdc.gov

BACKGROUND: Obesity is closely related to type 2 diabetes mellitus, and weight

reduction is an important part of the care delivered to obese persons with diabetes. The objective of this review was to assess the efficacy of pharmacotherapy for weight loss in adults with type 2 diabetes. METHODS: A systematic review of the literature was performed, and studies were included if pharmacotherapy was used as the primary strategy for weight loss among adults with type 2 diabetes. Published and unpublished studies with any design were included. A random effects model was used to combine outcomes from randomized controlled trials. RESULTS: Sufficient data for the meta-analysis were available for fluoxetine, orlistat, and sibutramine. Fourteen randomized, placebo-controlled trials were included in the review, with a total of 2231 patients. Pharmacotherapy produced modest reductions in weight for fluoxetine (3.4 kg [95% confidence interval (CI), 1.7-5.2 kg] at 8-16 weeks of follow-up; 5.1 kg [95% CI, 3.3-6.9 kg] at 24-30 weeks; and 5.8 kg [95% CI, 0.8-10.8 kg] at 52 weeks); orlistat (2.6 kg [95% CI, 2.1-3.2 kg] [2.6% loss] at 52 weeks); and sibutramine (4.5 kg [95% CI, 1.8-7.2 kg] [3.3% loss] at up to 26 weeks). Glycated hemoglobin was also modestly reduced: fluoxetine (1.0% [95% CI, 0.4%-1.5%] at 8-16 weeks; 1.0% [95% CI, 0.6%-1.4%] at 24-30 weeks; and 1.8% [95% CI, -0.2%-3.8%] at 52 weeks); orlistat (0.4% [95% CI, 0.3%-0.5%]); and sibutramine (0.7% [95% CI, -0.5%-1.9%]). Gastrointestinal adverse effects were common with orlistat; tremor, somnolence, and sweating with fluoxetine; and palpitations with sibutramine. CONCLUSIONS: Fluoxetine, orlistat, and sibutramine can achieve statistically significant weight loss over 26 to 52 weeks. However, the magnitude of weight loss was modest, and the long-term health benefits and safety remain unclear. Interventions that combine pharmacologic therapy with intensive behavioral interventions may be more effective but need additional research.

Publication Types:

Review

Review, Academic

PMID: 15249348 [PubMed - indexed for MEDLINE]

13: Br J Anaesth. 2004 Sep;93(3):343-7. Epub 2004 Jun 25.

Moderate hypothermia for 359 operations to clip cerebral aneurysms.

Kimme P, Fridrikssen S, Engdahl O, Hillman J, Vegfors M, Sjoberg F.

Department of Anaesthesiology and Intensive Care, Faculty of Health Sciences,

University Hospital, S-581 85 Linköping, Sweden. Peter.Kimme@lio.se

BACKGROUND: Experimental data have suggested that hypothermia (32-34 degrees C)

may improve outcome after cerebral ischaemia, but its efficacy has not yet been established conclusively in humans. In this study we examined the feasibility and safety of deliberate moderate perioperative hypothermia during operations for subarachnoid aneurysms. METHODS: A total of 359 operations for intracranial cerebral aneurysms were included in this prospective study. By using cold intravenous infusions (4 degrees C) and convective cooling our aim was to reduce the patient's core temperature to more than 34 degrees C within 1 h before operation. The protocol assessed postoperative complications such as infections, prolonged mechanical ventilation, pulmonary complications and coagulopathies. RESULTS: During surgery, the body temperature was reduced to a mean of 32.5 (SD 0.4) degrees C. Cooling was accomplished at a rate of 4.0 (SD 0.4) degrees C h(-1). All patients were normothermic at 5 (sd 2) h postoperatively. Peri/postoperative complications included circulatory instability (n=36, 10%), arrhythmias (n=17, 5%) coagulation abnormalities and blood transfusion (n=169, 47%), infections (n=29, 8%) and pulmonary complications (infiltrate or oedema

while on ventilatory support) (n=97, 27%). Eighteen patients died within 30 days (5%). There was no significant correlation between the extent of hypothermia and any of the complications. However, there was a strong correlation between the occurrence of complications and the severity of the underlying neurological disease as assessed by the Hunt and Hess score. CONCLUSION: Moderate hypothermia

accomplished within 1 h of induction of anaesthesia and maintained during surgery for subarachnoid aneurysms appears to be a safe method as far as the risks of peri/postoperative complications such as circulatory instability, coagulation abnormalities and infections are concerned.

Publication Types:

Evaluation Studies

PMID: 15220173 [PubMed - indexed for MEDLINE]

14: Br J Haematol. 2004 Jul;126(1):127-32.

Efficacy and safety of two different rG-CSF preparations in the treatment of patients with severe congenital neutropenia.

Carlsson G, Ahlin A, Dahllof G, Elinder G, Henter JI, Palmblad J.

Department of Woman and Child Health, Childhood Cancer Research Unit, Karolinska Hospital, Karolinska Institute, Stockholm, Sweden. goran.carlsson@kbh.ki.se

In patients with severe congenital neutropenia (SCN), the absolute neutrophil count (ANC) is raised during treatment with granulocyte colony-stimulating factor (G-CSF), resulting in a marked reduction of bacterial infection. Some patients, however, still have recurrent but less severe bacterial infections and severe periodontal infections. As it has been suggested that the biological activity of glycosylated recombinant human G-CSF (rHuG-CSF, i.e. lenograstim) is higher than the non-glycosylated form (i.e. filgrastim), we compared the two given in equimolar doses. Seven SCN patients participated in an open, randomized, double crossover study comprising 60 weeks, with four 12-week periods when the two drugs alternated after a 12-week run-in-period. The mean ANC values, sampled every second week, were  $5.1 \times 10^9/l$  during filgrastim treatment and  $4.2 \times 10^9/l$  during lenograstim treatment ( $P = 0.042$ ). The ANC levels were also significantly higher during filgrastim treatment, when comparing each complementary pair of ANC measurements ( $P = 0.011$ ) as well as the mean ANC values during each 12-week treatment period ( $P = 0.033$ ). There were no differences regarding the frequency of infection, antibiotic treatment, gingival bleeding and the number of hospital admissions between the groups. We conclude that filgrastim and lenograstim displayed equal clinical efficacy, but that ANC levels were higher during filgrastim treatment, when administered in equimolar doses.

Publication Types:

Clinical Trial

Randomized Controlled Trial

PMID: 15198743 [PubMed - indexed for MEDLINE]

14: Br J Psychiatry. 2004 Jul;185:3-4.

Improving safety in medicine: a systems approach.

Munro E.

Publication Types:

Editorial

PMID: 15231548 [PubMed - indexed for MEDLINE]

15: Cancer Immunol Immunother. 2004 Sep;53(9):777-85. Epub 2004 Jun 08.

Dendritic cells can be rapidly expanded ex vivo and safely administered in patients with metastatic breast cancer.

Dees EC, McKinnon KP, Kuhns JJ, Chwastiak KA, Sparks S, Myers M, Collins EJ, Frelinger JA, Van Deventer H, Collichio F, Carey LA, Brecher ME, Graham M, Earp HS, Serody JS.

Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Campus Box #7295, Chapel Hill, NC 27599-7295, USA.

**PURPOSE:** Immunotherapy using either dendritic cells (DCs) or expanded cytotoxic T cells (CTLs) has received increased interest in the treatment of specific malignancies including metastatic breast cancer (MBC). DCs can be generated ex vivo from monocytes or CD34+ precursors. The ability to expand and safely administer CD34-derived DCs in patients with MBC that have received prior cytotoxic chemotherapy has not been evaluated. **METHODS:** We enrolled ten patients with MBC that had received prior chemotherapy for the treatment of metastatic disease on a phase I/II trial designed to test the safety and feasibility of administering ex vivo expanded DCs from CD34+ progenitor cells. **RESULTS:** Using a cocktail of multiple different cytokines, we could expand DCs 19-fold compared to the initial CD34-selected product, which allowed the administration of as many as six vaccine treatments per patient. Patients received three to six injections i.v. of DCs pulsed with either the wild type GP2 epitope from the HER-2/neu protein or an altered peptide ligand, isoleucine to leucine (I2L). Toxicity was mild, with no patients demonstrating grade III toxicity during the treatment. Two patients with subcutaneous disease had a partial response to therapy, while IFN-gamma-producing CD8+ T cells could be found in two other patients during treatment. **CONCLUSIONS:** This approach is safe and effective in generating a significant quantity of DCs from CD34-precursors.

PMID: 15185007 [PubMed - indexed for MEDLINE]

16: Colorectal Dis. 2004 Jul;6(4):254-7.

Restorative proctectomy after emergency laparoscopic colectomy for ulcerative colitis: a case-matched study.

Maartense S, Dunker MS, Slors JF, Gouma DJ, Bemelman WA.

Department of Surgery, Academic Medical Centre, Amsterdam, The Netherlands.

**OBJECTIVE:** The aim of the study was to evaluate feasibility and safety of restorative proctectomy with ileal pouch anal anastomosis (IPAA) through a Pfannenstiel incision after prior laparoscopic colectomy. **METHODS:** Seventeen patients who underwent restorative proctectomy after laparoscopic emergency colectomy for ulcerative colitis (UC) were prospectively evaluated. Results were compared with results of a group of 21 case matched patients that had restorative proctectomy and IPAA via a midline incision in the same period. **RESULTS:** Median operation time was longer, although not significantly, in patients who had a restorative proctectomy through a pfannenstiel (186 min) compared to a restorative proctectomy through a midline incision (158 min). Procedure related complications were comparable between the groups, respectively, 1 of 17 patients in the pfannenstiel group and 3 of 21 patients in the median laparotomy group. Median hospital stay in the pfannenstiel group was 10 days and in the midline group 12 days. **CONCLUSIONS:** After laparoscopic assisted emergency colectomy for ulcerative colitis, restorative proctectomy is feasible and can be performed safely through a Pfannenstiel incision.

PMID: 15206968 [PubMed - indexed for MEDLINE]

17: Curr Opin Lipidol. 2004 Aug;15(4):453-7.  
Statin therapy in the elderly.  
Mungall MM, Gaw A.  
Clinical Trials Unit, Glasgow Royal Infirmary, Glasgow, UK.

**PURPOSE OF REVIEW:** The clinical efficacy and safety of statin therapy have been well established from a series of large-scale, randomized controlled trials. These trials, however, have predominantly recruited patients under the age of 70 years. As a consequence, the use of statins in older patients has remained controversial. **RECENT FINDINGS:** The results of the first trial to look exclusively at the elderly--the Prospective Study of Pravastatin in the Elderly at Risk--have added enormously to our understanding of the use of statins in the elderly. These findings, together with those from the large elderly cohort within the Heart Protection Study and the smaller elderly subgroups within the other major statin trials, have forced us to re-evaluate any systematic exclusion of elderly patients from statin therapy. **SUMMARY:** The collective evidence now strongly supports the use of statins in the at-risk elderly population.

Publication Types:  
Review  
Review, Tutorial

PMID: 15243219 [PubMed - indexed for MEDLINE]

18: Dis Esophagus. 2004;17(1):95-7.  
Laparoscopic inversion esophagectomy: simplifying a daunting operation.  
Jbe BA, Reavis KM, Davis JJ, Hunter JG.  
Department of Surgery, Oregon Health and Science University, Portland VA Medical Center, Portland, Oregon 97207, USA. jobeb@ohsu.edu  
Minimally invasive esophageal resection is a technically demanding procedure that may reduce patient morbidity and improve convalescence when compared with the open approach. Despite these proposed advantages, the minimally invasive approach has not been widely embraced and is routinely performed in only a few specialized centers around the world. The laparoscopic inversion esophagectomy attempts to eliminate some of the technical obstacles inherent in this procedure by simplifying the transhiatal mediastinal dissection, facilitating vagal preservation, and enhancing safety. We present a case of a 37-year-old man who underwent laparoscopic inversion esophagectomy for Barrett's esophagus with high-grade dysplasia. Immediate and long-term outcome measures are being prospectively gathered in order to establish the ultimate value of this procedure. Copyright 2004 ISDE

Publication Types:  
Case Reports

PMID: 15209750 [PubMed - indexed for MEDLINE]

19: Drug Saf. 2004;27(8):555-67.  
A problem-oriented approach to safety issues in drug development and beyond.  
Haas JF.  
Pharmacovigilance, Genzyme Corporation, Cambridge, Massachusetts 02142, USA.  
joanna.haas@genzyme.com  
Human safety issues arise throughout the life cycle of pharmaceutical products and relevant information comes from a multitude of sources. Assessment and

management of risks to humans requires a problem-based analysis to bring together relevant information regardless of source. The Safety Evaluation Plan (SEP) is a tool to support problem-oriented safety analysis. Safety issues are specified and the evaluation and management of each problem is based on a status summary that integrates the most current information from all relevant sources. The status summary is updated regularly during the course of clinical development to reflect the results of new studies and new clinical trials. In the postmarketing period, relevant postmarketing data is incorporated. Recent regulatory initiatives emphasise early identification of product safety risks so that appropriate risk-management measures can be instituted at the time of approval. A problem-oriented approach supports growing regulatory expectations regarding risk assessment and risk management. The problem-oriented approach facilitates early identification of safety issues and an evidence-based approach to their evaluation. Proactive management of safety problems leads to prompt assessment of risks and timely and appropriate steps aimed at risk reduction. The SEP provides a single global assessment for each safety issue. Regulatory submissions for pharmaceutical and biological products are organised by type of information. International Conference of Harmonisation documents covering clinical safety issues structure and analyse information separately by type, for example, adverse events, serious adverse events, laboratory data, vital signs, etc. A problem-oriented analysis would need to find a place in the regulatory process. A problem-oriented approach to safety cuts across typical structures in the pharmaceutical industry where different groups handle preclinical, clinical and postmarketing safety information. The SEP can improve communication within the company and externally. Nonetheless, supporting structures need to be adapted to support such an interdisciplinary process. Overall, the problem-oriented approach, supported by a SEP, contributes to realistic expectations and sustained credibility when dealing with safety issues.

Publication Types:

Review

Review, Tutorial

PMID: 15154827 [PubMed - indexed for MEDLINE]

20: Drug Saf. 2004;27(8):509-17.

CIOMS and ICH initiatives in pharmacovigilance and risk management: overview and implications.

Tsintis P, La Mache E.

European Agency for the Evaluation of Medicinal Products, London, United Kingdom. Panos.Tsintis@emea.eu.int

In this article we review the current initiatives by the Council for International Organizations of Medical Sciences (CIOMS) and the International Conference on Harmonisation (ICH) on pharmacovigilance planning that are due for general release during 2004. These initiatives could form the basis for applying concepts of risk management to medicines throughout their life cycle, from preclinical and clinical development to marketed use. The CIOMS VI Working Group (with 28 senior scientists worldwide from drug regulatory authorities and pharmaceutical companies) is currently developing scientific guidance that relates to clinical trials for medicines during development. It recommends a developmental pharmacovigilance concept - a 'living' concept that would start early in drug development supporting the science and ethics of research leading up to licensing (marketing authorisation) and continuing to post-authorisation (postmarketing) pharmacovigilance. This approach is seen as complementary to current ICH initiatives called 'Pharmacovigilance Planning'. ICH will introduce two concepts in pharmacovigilance management of medicinal products: the

'Pharmacovigilance Specification' and the 'Pharmacovigilance Plan'. The 'Pharmacovigilance Specification' will summarise important knowns and unknowns about the medicine. It will include safety risks identified at the licensing stage, potential risks and any key missing information. These elements will be essential to the formulation of pharmacovigilance plans. Dialogue and common understanding between regulators and the pharmaceutical industry will be a key factor for developing pharmacovigilance plans during the life cycle of medicines. Appropriate interaction with health professionals and patients should also be planned for the future as regulatory systems become more transparent. Where no significant issues are apparent at the licensing (marketing authorisation) stage, routine pharmacovigilance practices will be followed during the marketing phase. Where issues do exist or the data are limited, further study, including epidemiological approaches can be planned. All types of medicines (new drugs, biological agents, orphan drugs) may be involved in these concepts, as would major extensions to existing medicines. Currently ongoing CIOMS and ICH initiatives are in line with emerging risk-management strategies in the US, the European Union and Japan aimed at early and proactive pharmacovigilance.

Publication Types:

Review  
Review, Tutorial

PMID: 15154824 [PubMed - indexed for MEDLINE]

21: Drugs Aging. 2004;21(8):485-98.

Over-the-counter analgesics in older adults: a call for improved labelling and consumer education.

Roumie CL, Griffin MR.

Quality Scholars Program, Veterans Administration, Tennessee Valley Healthcare System, Nashville, Tennessee 37212, USA. christianne.roumie@vanderbilt.edu

The use of analgesics increases with age and on any given day 20-30% of older adults take an analgesic medication. Over-the-counter (OTC) analgesics are generally well tolerated and effective when taken for brief periods of time and at recommended dosages. However, their long-term use, use at inappropriately high doses, or use by persons with contraindications may result in adverse effects, including gastrointestinal haemorrhage, cardiovascular toxicity, renal toxicity and hepatotoxicity. Many OTC drugs are also available through a prescription, for a broader range of indications and for longer durations of use and wider dose ranges, under the assumption that healthcare providers will help patients make safe choices about analgesics. Safe and effective use of medications is one of the greatest challenges faced by healthcare providers in medicine. More than 60% of people cannot identify the active ingredient in their brand of pain reliever. Additionally, about 40% of Americans believe that OTC drugs are too weak to cause any real harm. As a result of a recent US FDA policy, the conversion of prescription to OTC medications will result in a 50% increase of OTC medications. To reduce the risks of potential adverse effects from OTC drug therapy in older adults, we propose that the use of analgesics will be enhanced through the use of patient and healthcare provider education, as well as improved labelling of OTC analgesics. Improved labelling of OTC analgesics may help consumers distinguish common analgesic ingredients in a wide variety of preparations and facilitate informed decisions concerning the use of OTC drugs. Copyright 2004 Adis Data Information BV

Publication Types:

Review  
Review, Tutorial

PMID: 15182214 [PubMed - indexed for MEDLINE]

22: Menopause. 2004 Jul-Aug; 11(4): 405-15.

Once-weekly alendronate 70 mg and raloxifene 60 mg daily in the treatment of postmenopausal osteoporosis.

Luckey M, Kagan R, Greenspan S, Bone H, Kiel RD, Simon J, Sackarowitz J, Palmisano J, Chen E, Petruschke RA, de Papp AE.

St. Barnabas Osteoporosis & Metabolic Bone Disease Center, Livingston, NJ, USA.

**OBJECTIVE:** To compare the efficacy and tolerability of once-weekly (OW) alendronate (ALN) 70 mg and raloxifene (RLX) 60 mg daily in the treatment of postmenopausal osteoporosis. **DESIGN:** This 12-month, randomized, double-blind study enrolled 456 postmenopausal women with osteoporosis (223 ALN, 233 RLX) at 52 sites in the United States. Efficacy measurements included lumbar spine (LS), total hip, and trochanter bone mineral density (BMD) at 6 and 12 months, biochemical markers of bone turnover, and percent of women who maintained or gained BMD in response to treatment. The primary endpoint was percent change from baseline in LS BMD at 12 months. Adverse experiences were recorded to assess treatment safety and tolerability. **RESULTS:** Over 12 months, OW ALN produced a significantly greater increase in LS BMD (4.4%,  $P < 0.001$ ) than RLX (1.9%). The percentage of women with  $\geq 0\%$  increase in LS BMD (ALN, 94%; RLX, 75%;  $P < 0.001$ ) and  $\geq 3\%$  increase in LS BMD (ALN, 66%; RLX, 38%;  $P < 0.001$ ) were significantly greater with ALN than RLX. Total hip and trochanter BMD increases were also significantly greater ( $P < 0.001$ ) with ALN. Greater ( $P < 0.001$ ) reductions in N-telopeptide of type I collagen and bone-specific alkaline phosphatase were achieved with ALN compared with RLX at 6 and 12 months. No significant differences in the incidence of upper gastrointestinal or vasomotor adverse experiences were seen. **CONCLUSION:** ALN 70 mg OW produced significantly greater increases in spine and hip BMD and greater reductions in markers of bone turnover than RLX over 12 months. A greater percentage of women maintained or gained BMD on ALN than RLX. Both medications had similar safety and tolerability profiles.

Publication Types:

Clinical Trial

Multicenter Study

Randomized Controlled Trial

PMID: 15243278 [PubMed - indexed for MEDLINE]

23: Occup Health Saf. 2004 Jun; 73(6): 52-4, 56.

Rings of protection: reducing your vulnerability to a terrorist attack.

Bennett B.

PMID: 15232908 [PubMed - indexed for MEDLINE]

24: Occup Health Saf. 2004 Jun; 73(6): 24-6.

Integrated injury intervention.

Rittenberry R.

PMID: 15232907 [PubMed - indexed for MEDLINE]

25: Occup Med (Lond). 2004 Jun;54(4):245-9.

Analysing and interpreting routinely collected data on sharps injuries in assessing preventative actions.

Moens G, Mylle G, Johannik K, Van Hoof R, Helsen G.

Department of Research & Development, External Service for Prevention and Protection at Work (IDEWE), Leuven, Belgium. guido.moens@idewe.be

**BACKGROUND:** Sharps injuries (SI) occur frequently in hospitals and are a risk for exposure to bloodborne pathogens. During the 1990s, the safety service of a university general hospital introduced, in collaboration with the occupational health service, specific measures to reduce the number of SI. **AIM:** The aim of this study was to assess the occurrence and evolution of SI during this period and to evaluate the effectiveness of the preventative measures taken, making use of routinely collected data. **METHOD:** In a retrospective study, we analysed the number of SI recorded from 1990 to 1997. The study population was all employees at risk of SI. Because the introduction of intensive preventative measures dates from 1996, an effect on the incidence of SI can be expected from 1996. To assess this effect, mean incidence rates for 1990-1995 and for 1996-1997 were compared. **RESULTS:** In the study period, a total of 4230 SI were recorded. The global SI incidence rate decreased from 33.4 SI per 100 occupied beds per year in 1990-1995 to 30.1 in 1996-1997 ( $P < 0.01$ ). In the same period, among nurses a decrease in incidence rate from 17.2 to 12.7 SI per 100 person-years was noted ( $P < 0.0001$ ) and for the hotel service from 4.8 to 3.7 (not significant). **CONCLUSION:** Although this study has various restraints, these results suggest that intensive preventative actions, in combination with technological advances, may have contributed to a drop of 67 SI cases per year.

PMID: 15190161 [PubMed - indexed for MEDLINE]

26: Pharmacoepidemiol Drug Saf. 2004 Jun;13(6):355-63.

Introducing triage logic as a new strategy for the detection of signals in the WHO Drug Monitoring Database.

Stahl M, Lindquist M, Edwards IR, Brown EG.

Uppsala Monitoring Centre, Uppsala, Sweden.

**PURPOSE:** An important role for the WHO Programme for International Drug Monitoring is to identify signals of international drug safety problems as early as possible. The signal detection strategy, operated at the Uppsala Monitoring Centre (UMC), gave too many drug-adverse drug reaction (ADR) combinations for individual review. Therefore additional selection strategies were needed to improve the likely signal-to-noise ratio and for the UMC to complement the efforts of national centres in an efficient way. **METHODS:** The combinations database of the first quarter of 2001 was analysed using algorithms representing different strategies for finding relevant signals using triage logic. **RESULTS:** The strategies that together gave a manageable number of combinations, i.e. around 600, for further consideration in a single quarter were the algorithms for 'Rapid reporting increase', 'Serious reaction and new drug' and 'Special interests'. These filters began to be used routinely on the combinations database in late 2001. **CONCLUSIONS:** While stressing that human review is essential, triage strategies are useful when attempting analysis of large amounts of data. By definition, the use of triage strategies may exclude some potential signals from consideration, although the intention is to improve the chances of detection by focussing on areas of greatest importance. Copyright

2004 John Wiley & Sons, Ltd.

PMID: 15170764 [PubMed - indexed for MEDLINE]

27: Soc Sci Med. 2004 Sep;59(5):915-30.

Responses of established healthcare to the professionalization of complementary and alternative medicine in Ontario.

Kelner M, Wellman B, Boon H, Welsh S.

Institute for Human Development, Life Course and Aging, University of Toronto, 222 College St, Ste 106, Toronto, Canada M5 T 3J1. bevwell@chass.utoronto.ca

This paper examines the reactions of leaders of established health professions in Ontario, Canada to the efforts of selected complementary and alternative (CAM) occupational groups (chiropractors, naturopaths, acupuncture/traditional Chinese doctors, homeopaths and Reiki practitioners) to professionalize. Stakeholder theory provides the framework for analysis of competing interests among the various groups in the healthcare system. The data are derived from personal interviews with 10 formal leaders from medicine, nursing, physiotherapy, clinical nutrition and public health. We conceived of these leaders as one group of stakeholders, with both common and conflicting interests. The findings demonstrate that these stakeholders are reluctant to endorse the professionalization of CAM. They propose a series of strategies to contain the acceptance of CAM groups, such as insisting on scientific evidence of safety and efficacy, resisting integration of CAM with conventional medicine and opposing government support for research and education. These strategies serve to protect the dominant position of medicine and its allied professions, and to maintain existing jurisdictional boundaries within the healthcare system. The popular support for CAM will require that health professional stakeholders continue to address the challenges this poses, and at the same time protect their position at the apex of the healthcare pyramid.

PMID: 15186894 [PubMed - indexed for MEDLINE]

28: Virus Res. 2004 Jul;103(1-2):139-45.

Virosomal influenza vaccine: a safe and effective influenza vaccine with high efficacy in elderly and subjects with low pre-vaccination antibody titers.

de Bruijn IA, Nauta J, Gerez L, Palache AM.

Solvay Pharmaceuticals BV, Clinical Development, P.O. Box 900, 1380 DA Weesp, The Netherlands. iris.debruijn@solvay.com

In 14 clinical studies, various efficacy and safety aspects of a new virosomal influenza vaccine (Invivac) were assessed in 2865 subjects. The virosomal influenza vaccine fully complies with the Committee for Proprietary Medicinal Products (CPMP) requirement for immunogenicity of influenza vaccines. In particular, in a subset of subjects with low pre-vaccination titers (thus those persons who actually need protection by a vaccine), between 76 and 99% of subjects (dependent on age, health status and vaccine components) achieved protective hemagglutination inhibiting (HI) antibody titers after vaccination with the virosomal influenza vaccine. Acceptable frequencies of well-known local and systemic reactions were observed in healthy adults and risk subjects in clinical studies and in a post-marketing study population. These reactions were transient and generally not severe, and did not cause major inconvenience. In conclusion, Invivac is an efficacious and safe vaccine for the protection against influenza in healthy and chronically ill adult subjects. The vaccine is especially efficacious in subjects with low pre-vaccination immunity.

Publication Types:  
Meta-Analysis

PMID: 15163502 [PubMed - indexed for MEDLINE]