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PERSPECTIVES


On September 6, 2007, Senators Charles Grassley (R-IA), the ranking member of the Committee on Finance, and Herb Kohl (D-WI), chairman of the Special Committee on Aging, introduced the Physician Payments Sunshine Act — so named because it aims to “shine a much needed ray of sunlight on a situation that contributes to the exorbitant cost of health care,” according to cosponsor Senator Charles Schumer (D-NY). The bill would require manufacturers of pharmaceuticals and medical devices with annual revenues of more than $100 million to disclose the amount of money they give to physicians — whether in the form of . . .


Since 1999, health care professionals have been focusing on To Err Is Human, the Institute of Medicine report that sounded alarms about medical error. As we have strived to reduce the rate of errors, systems-based practices such as electronic order entry and procedure checklists have proliferated. Meanwhile, little attention has been paid to the second half of the adage — “to forgive, divine.” How can we characterize and address the human dimensions of medical error so that patients, families, and clinicians may reach some degree of closure and move toward forgiveness? In interviews that our group conducted for a documentary . . .


Since 1994, inaction and incrementalism have governed U.S. health policy, with the predictable result that both health care spending and the number of uninsured Americans have reached record levels. Indeed, worsening conditions in the health care system have triggered renewed interest in comprehensive health care reform. Signs of change in the health care debate are everywhere — in the formation of coalitions by business and labor groups to pursue reform, the launching of advertising campaigns by the American Cancer Society and the American Medical Association to highlight the plight of the uninsured, the pursuit of ambitious plans by states such . . .

Who should protect the public? The supreme court and medical device regulation. New England Journal of Medicine, 357 (17), 1680-1681.

A decade ago, Charles Riegel was undergoing a coronary angioplasty procedure when a balloon catheter ruptured. Complete heart block developed, and Riegel lost consciousness and had to undergo emergency coronary bypass surgery. A U.S. Court of Appeals ruled that Riegel could not sue Medtronic, the manufacturer of the catheter, for his injuries and resulting disability. The Supreme Court recently agreed to review that holding and will hear oral arguments later this fall. Its decision is expected by June 2008. The technical issue in the case is the proper interpretation . . .

ABSTRACTS


The rate of hypoglycemia, and weight gain. At 1 year, mean glycated hemoglobin levels were similar in the biphasic group (7.3%) and the prandial group (7.2%) (P=0.08) but higher in the basal group (7.6%, P<0.001 for both comparisons). The respective proportions of patients with a glycated hemoglobin level of 6.5% or less were 17.0%, 23.9%, and 8.1%; respective mean numbers of hypoglycemic events per patient per year were 5.7, 12.0, and 2.3; and respective mean weight gains were 4.7 kg, 5.7 kg, and 1.9 kg. Rates of adverse events were similar among the three groups. A single analogue-insulin formulation added to metformin and sulfonylurea resulted in a glycated hemoglobin level of 6.5% or less in a minority of patients at 1 year. The addition of biphasic or prandial insulin aspart reduced levels more than the addition of basal insulin detemir but was associated with greater risks of hypoglycemia and weight gain.

Adding insulin to oral therapy in type 2 diabetes mellitus is customary when glycemic control is suboptimal, though evidence supporting specific insulin regimens is limited. In an open-label, controlled, multicenter trial, we randomly assigned 708 patients with a suboptimal glycated hemoglobin level (7.0 to 10.0%) who were receiving maximally tolerated doses of metformin and sulfonylurea to receive biphasic insulin aspart twice daily, prandial insulin aspart three times daily, or basal insulin detemir once daily (twice if required). Outcome measures at 1 year were the mean glycated hemoglobin level, the proportion of patients with a glycated hemoglobin level of 6.5% or less, the rate of hypoglycemia, and weight gain. At 1 year, mean glycated hemoglobin levels were similar in the biphasic group (7.3%) and the prandial group (7.2%) (P=0.08) but higher in the basal group (7.6%, P<0.001 for both comparisons). The respective proportions of patients with a glycated hemoglobin level of 6.5% or less were 17.0%, 23.9%, and 8.1%; respective mean numbers of hypoglycemic events per patient per year were 5.7, 12.0, and 2.3; and respective mean weight gains were 4.7 kg, 5.7 kg, and 1.9 kg. Rates of adverse events were similar among the three groups. A single analogue-insulin formulation added to metformin and sulfonylurea resulted in a glycated hemoglobin level of 6.5% or less in a minority of patients at 1 year. The addition of biphasic or prandial insulin aspart reduced levels more than the addition of basal insulin detemir but was associated with greater risks of hypoglycemia and weight gain.


Mortality is increased after a hip fracture, and strategies that improve outcomes are needed. In this randomized, double-blind, placebo-controlled trial, 1065 patients were assigned to receive yearly intravenous zoledronic acid (at a dose of 5 mg), and 1062 patients were assigned to receive placebo. The infusions were first administered within 90 days after surgical repair of a hip fracture. All patients (mean age, 74.5 years) received supplemental vitamin D and calcium. The median follow-up was 1.9 years. The primary end point was a new clinical fracture. The rates of any new clinical fracture were 8.6% in the zoledronic acid group and 13.9% in the placebo group, a 35% risk reduction with zoledronic acid (P=0.001); the respective rates of a new clinical vertebral fracture were 1.7% and 3.8% (P=0.02), and the respective rates of new nonvertebral fractures were 7.6% and 10.7% (P=0.03). In the safety analysis, 101 of 1054 patients in the zoledronic acid group (9.6%) and 141 of 1057 patients in the placebo group (13.3%) died, a reduction of 28% in deaths from any cause in the zoledronic acid group (P=0.01). The most frequent adverse events in patients receiving zoledronic acid were pyrexia, myalgia, and bone and musculoskeletal pain. No cases of osteonecrosis of the jaw were reported, and no adverse effects on the healing of fractures were noted. The rates of renal and cardiovascular adverse events, including atrial fibrillation and stroke, were similar in the two groups. An annual infusion of zoledronic acid within 90 days after repair of a low-trauma hip fracture was associated with a reduction in the rate of new clinical fractures and with improved survival.


A randomized phase 3 trial of the treatment of squamous-cell carcinoma of the head and neck compared induction chemotherapy with docetaxel plus cisplatin and fluorouracil (TPF) with cisplatin and fluorouracil (PF), followed by chemoradiotherapy. We randomly assigned 501 patients (all of whom had stage III or IV disease with no distant metastases and tumors considered to be unresectable or were candidates for organ preservation) to receive either TPF or PF induction chemotherapy, followed by chemoradiotherapy with weekly carboplatin.
therapy and radiotherapy for 5 days per week. The primary end point was overall survival. With a minimum of 2 years of follow-up years for 69% of patients, significantly more patients survived in the TPF group than in the PF group (hazard ratio for death, 0.70; P=0.006). Estimates of overall survival at 3 years were 62% in the TPF group and 48% in the PF group; the median overall survival was 71 months and 30 months, respectively (P=0.006). There was better locoregional control in the TPF group than in the PF group (P=0.04), but the incidence of distant metastases in the two groups did not differ significantly (P=0.14). Rates of neutropenia and febrile neutropenia were higher in the TPF group; chemotherapy was more frequently delayed because of hematologic adverse events in the PF group. Patients with squamous-cell carcinoma of the head and neck who received docetaxel plus cisplatin and fluorouracil induction chemotherapy plus chemoradiotherapy had a significantly longer survival than did patients who received cisplatin and fluorouracil induction chemotherapy plus chemoradiotherapy.

An out-of-body experience was repeatedly elicited during stimulation of the posterior part of the superior temporal gyrus on the right side in a patient in whom electrodes had been implanted to suppress tinnitus. Positron-emission tomographic scanning showed brain activation at the temporoparietal junction — more specifically, at the angular–supramarginal gyrus junction and the superior temporal gyrus–sulcus on the right side. Activation was also noted at the right precuneus and posterior thalamus, extending into the superior vermis. We suggest that activation of these regions is the neural correlate of the disembodiment that is part of the out-of-body experience.


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Advanced gastric cancer can respond to S-1, an oral fluoropyrimidine. We tested S-1 as adjuvant chemotherapy in patients with curatively resected gastric cancer. Patients in Japan with stage II or III gastric cancer who underwent gastrectomy with extended (D2) lymph-node dissection were randomly assigned to undergo surgery followed by adjuvant therapy with S-1 or to undergo surgery only. In the S-1 group, administration of S-1 was started within 6 weeks after surgery and continued for 1 year. The treatment regimen consisted of 6-week cycles in which, in principle, 80 mg of oral S-1 per square meter of body-surface area per day was given for 4 weeks and no chemotherapy was given for the following 2 weeks. The primary end point was overall survival. We randomly assigned 529 patients to the S-1 group and 530 patients to the surgery-only group between October 2001 and December 2004. The trial was stopped on the recommendation of the independent data and safety monitoring committee, because the first interim analysis, performed 1 year after enrollment was completed, showed that the S-1 group had a higher rate of overall survival than the surgery-only group (P=0.002). Analysis of follow-up data showed that the 3-year overall survival rate was 80.1% in the S-1 group and 70.1% in the surgery-only group. The hazard ratio for death in the S-1 group, as compared with the surgery-only group, was 0.68 (95% confidence interval, 0.52 to 0.87; P=0.003). Adverse events of grade 3 or grade 4 (defined according to the Common Toxicity Criteria of the National Cancer Institute) that were relatively common in the S-1 group were anorexia (6.0%), nausea (3.7%), and diarrhea (3.1%). S-1 is an effective adjuvant treatment for East Asian patients who have undergone a D2 dissection for locally advanced gastric cancer.


Phase 2 studies suggest that the standard regimen of cisplatin and fluorouracil (PF) plus docetaxel (TPF) improves outcomes in squamous-cell carcinoma of the head and neck. We compared TPF with PF as induction chemotherapy in patients with locoregionally advanced, unresectable disease. We randomly assigned eligible patients between the ages of 18 and 70 years who had stage III or stage IV disease and no distant metastases to receive either TPF (docetaxel and cisplatin, day 1; fluorouracil by continuous infusion, days 1 to 5) or...
PF every 3 weeks for four cycles. Patients without progression of disease received radiotherapy within 4 to 7 weeks after completing chemotherapy. The primary end point was progression-free survival. A total of 358 patients underwent randomization, with 177 assigned to the TPF group and 181 to the PF group. At a median follow-up of 32.5 months, the median progression-free survival was 11.0 months in the TPF group and 8.2 months in the PF group (hazard ratio for disease progression or death in the TPF group, 0.72; P=0.007). Treatment with TPF resulted in a reduction in the risk of death of 27% (P=0.02), with a median overall survival of 18.8 months, as compared with 14.5 months in the PF group. There were more grade 3 or 4 events of leukopenia and neutropenia in the TPF group and more grade 3 or 4 events of thrombocytopenia, nausea, vomiting, stomatitis, and hearing loss in the PF group. The rates of death from toxic effects were 2.3% in the TPF group and 5.5% in the PF group. As compared with the standard regimen of cisplatin and fluorouracil, induction chemotherapy with the addition of docetaxel significantly improved progression-free and overall survival in patients with unresectable squamous-cell carcinoma of the head and neck.


Magnetic resonance imaging (MRI) of the brain is increasingly used both in research and in clinical medicine, and scanner hardware and MRI sequences are continually being improved. These advances are likely to result in the detection of unexpected, asymptomatic brain abnormalities, such as brain tumors, aneurysms, and subclinical vascular pathologic changes. We conducted a study to determine the prevalence of such incidental brain findings in the general population. The subjects were 2000 persons (mean age, 63.3 years; range, 45.7 to 96.7) from the population-based Rotterdam Study in whom high-resolution, structural brain MRI (1.5 T) was performed according to a standardized protocol. Two trained reviewers recorded all brain abnormalities, including asymptomatic brain infarcts. The volume of white-matter lesions was quantified in milliliters with the use of automated postprocessing techniques. Two experienced neuroradiologists reviewed all incidental findings. All diagnoses were based on MRI findings, and additional histologic confirmation was not obtained. Asymptomatic brain infarcts were present in 145 persons (7.2%). Among findings other than infarcts, cerebral aneurysms (1.8%) and benign primary tumors (1.6%), mainly meningiomas, were the most frequent. The prevalence of asymptomatic brain infarcts and meningiomas increased with age, as did the volume of white-matter lesions, whereas aneurysms showed no age-related increase in prevalence. Incidental brain findings on MRI, including subclinical vascular pathologic changes, are common in the general population. The most frequent are brain infarcts, followed by cerebral aneurysms and benign primary tumors. Information on the natural course of these lesions is needed to inform clinical management.


Hepatitis A vaccine administered to persons after exposure to the hepatitis A virus has not been compared directly with immune globulin, which is known to be highly effective in preventing hepatitis A when given within 2 weeks after exposure to the virus. We randomly assigned household and day-care contacts, 2 to 40 years of age, in Almaty, Kazakhstan, to receive one standard age-appropriate dose of hepatitis A vaccine or immune globulin within 14 days after exposure to patients with hepatitis A. Instances of laboratory-confirmed, symptomatic hepatitis A infection occurring between 15 and 56 days after exposure were then assessed during active follow-up of all susceptible contacts. Of 4524 contacts who underwent randomization, 1414 (31%) were susceptible to hepatitis A virus and 1090 were eligible for the per-protocol analysis. Among these contacts, 568 received hepatitis A vaccine and 522 received immune globulin. Most contacts were children (average age, 12 years), and most received prophylaxis during the second week after exposure (average interval after exposure, 10 days). The baseline characteristics of the contacts were similar in the two groups. Symptomatic infection with hepatitis A virus was confirmed in 25 contacts receiving vaccine (4.4%) and in 17 contacts receiving immune globulin (3.3%) (relative risk, 1.35; 95% confidence interval, 0.70 to 2.67). Low rates of hepatitis A in both groups indicate that hepatitis A vaccine and immune globulin provided good protection after exposure. Although the study's prespecified criterion for noninferiority was met, the slightly higher rates of hepatitis A among vaccine recipients may indicate a true modest difference in efficacy and might be clinically meaningful in
some settings. Vaccine has other advantages, including long-term protection, and it may be a reasonable alternative to immune globulin for postexposure prophylaxis in many situations.

REVIEW ARTICLE


Celiac disease is a unique autoimmune disorder, unique because the environmental precipitant is known. The disorder was previously called celiac sprue, based on the Dutch word sprue, which was used to describe a disease similar to tropical sprue that is characterized by diarrhea, emaciation, aphthous stomatitis, and malabsorption.1,2 Celiac disease is precipitated, in genetically predisposed persons, by the ingestion of gluten, the major storage protein of wheat and similar grains.3 Originally considered a rare malabsorption syndrome of childhood, celiac disease is now recognized as a common condition that may be diagnosed at any age and that affects many organ systems. . .


Leukotrienes (“leuko,” from white blood cells; and “trienes,” three conjugated double bonds) comprise a family of products of the 5-lipoxygenase pathway of arachidonic acid metabolism. The cysteinyl leukotrienes C4, D4, and E4 account for the biologic activity that was previously termed “slow-reacting substance of anaphylaxis,” and the efficacy of antagonists to type 1 cysteinyl leukotriene receptor (CysLT1) in asthma validates the importance of cysteinyl leukotrienes and CysLT1 in this disease.1 This article reviews both established understanding and recent advances in our knowledge about leukotrienes.

IMAGES IN CLINICAL MEDICINE


A 9-year-old girl with recurrent respiratory infection presented for evaluation for possible active tuberculosis. Multislice computed tomography of the chest showed no evidence of active tuberculosis, but there was an incidental finding of a tracheal bronchus (shown with black arrow on the volume-rendering reconstruction, along with the right main bronchus [arrowhead] and left main bronchus [white arrow], and on the virtual-bronchoscopy inset [arrow], along with the tracheal carina [arrowhead]). A tracheal bronchus is an aberrant bronchus that arises most often from the right tracheal wall above the carina and supplies the right upper lobe. The prevalence ranges from 0.1 to . . .


A 68-year-old man with a history of asthma and chronic obstructive pulmonary disease was admitted to our hospital with a 1-day history of dyspnea, fever, and epigastric and chest pain. Shortly after admission, the patient’s hypoxemia became progressively worse and abdominal tenderness developed; he was admitted to the intensive care unit (ICU). Urgent computed tomography of the abdomen and pelvis showed a distended segment of the small bowel, with a mass causing obstruction. On emergency laparotomy, an obstruction due to a food bolus 7 cm in length was found and removed. Multiorgan failure and the acute respiratory distress syndrome developed . . .


A 69-year-old man presented with a 10-day history of discoloration of the left foot and pain in the left foot while at rest. He reported a 1-year history of intermittent claudication in his left leg. His medical history was notable for type 2 diabetes mellitus and hypertension. On examination, his left foot was erythematous, cold to the touch, and pulseless in the dorsalis pedis and posterior tibial arteries while hanging down (Panel A). However, the foot became pale when elevated (Panel B) and became red again while hanging down, which is Buerger’s symptom, suggesting the presence of peripheral artery disease. . . .


An 80-year-old woman with a myopia of –19.0 diopters and a history of right-sided retinal detachment underwent a diagnostic workup for a decrease of vision in her right eye. The visual acuity of the right eye had decreased from 20/100 to the perception of light only, and the left eye was unaffected. Ophthalmoscopy suggested a total retinal and choroidal detachment of unclear cause. Magnetic resonance imaging was performed to rule out an underlying neoplasm. The contrast-enhanced coronal and transverse T1-weighted images (Panels A and B, respectively) showed an unusual appearance of retinal detachment: a symmetrical bulging, resulting in a . . .
CLINICAL PRACTICE


This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author’s clinical recommendations. A 75-year-old woman with type 2 diabetes mellitus and peripheral vascular disease is admitted with a gangrenous ulcer of the plantar aspect of her left foot. A surgical consultation results in a recommendation for a below-the-knee amputation, but the patient declines the procedure on the grounds that she has lived long enough and wants to die with her body intact . . .

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL


A 49-year-old man infected with the human immunodeficiency virus (HIV) was seen in the hematology clinic at this hospital for evaluation of anemia. Five weeks earlier (1 week before a routine follow-up visit with his infectious-disease specialist), laboratory testing showed anemia (Table 1). Treatment with iron and multiple vitamins was initiated, and the patient was referred for hematologic evaluation. The long-term fiscal condition of the United States has been largely misdiagnosed. Despite all the attention paid to demographic challenges, such as the coming retirement of the baby-boom generation, our country’s financial health will in fact be determined primarily by the growth rate of per capita health care costs.

CLINICAL PROBLEM-SOLVING

Don R. Martin, D. William Schlott, and John A. Flynn. (2007). No respecter of age: a previously healthy 65-year-old woman went to her primary care physician in late August, seeking evaluation of a “spot” that had appeared on her right leg 3 weeks earlier. She felt completely well and recalled no trauma or tick bites. Her physical examination was notable only for a low-grade temperature elevation (37.7°C) and a 7-to-8-mm erythematous macule on her right leg. She . . .