Permanente Abstracts

Most of the abstracts in this issue focus on epidemiological studies that have direct clinical applications. They elucidate the factors that improve patient care and enhance health. The first group of studies includes cancer diagnosis and prevention, and antibiotic therapy for bronchitis. The second group of abstracts describes factors that influence trends in several diseases.

Permanente physicians are conducting important studies that demonstrate the use and value of guidelines for clinical practice. For this, they rely on Kaiser Permanente data to determine how closely clinical care conforms to expert recommendations and clinical trial results. Interestingly, regarding the management of acute bronchitis, data suggest that clinicians are not following these results and recommendations.

The utility of these existing guidelines, assessed with Kaiser Permanente data, represents review of large clinical populations. KP researchers also use these large databases to track the impact of care delivery interventions and their related costs and benefits. In addition, findings from research at KP have implications for public health policy far outside the immediate scope of Permanente practice.

Thus, this abstract section cuts across many areas of medicine and focuses on a large and diverse sector of the public health and well-being. Clearly, the KP databases and researchers make a significant contribution to increasing our knowledge about health and the factors that can improve clinical practice.

Evaluation of Excessive Anticoagulation in a Group Model Health Maintenance Organization

Lousberg TR; Witt DM; Beall DG; Carter BL; Malone DC; Arch Intern Med 1998 Mar 9;158(5):528-34.

Background: The fourth American College of Chest Physicians Consensus Conference on Antithrombotic Therapy recently published guidelines that included recommendations regarding the management of excessive anticoagulation. Limited data are available to support these recommendations.

Objectives: To assess management and outcomes of excessive anticoagulation in a group model health maintenance organization, compare management with the published guidelines, and analyze the cost of treatment strategies.

Methods: A search of computerized laboratory information identified patients with an international normalized ratio (INR) of greater than 6.0 during the 9-month study. Pertinent data were collected through a retrospective medical record review. Information was concurrently collected for cost analyses.

Results: The analysis included 301 episodes of excessive anticoagulation among 248 patients. Most (83%) episodes of elevated INRs were managed conservatively by a temporary discontinuation of warfarin sodium therapy until the INR was in a therapeutic range. Conservative management resulted in no sequelae in 212 (85.1%) of 249 episodes. Two episodes (0.8%) of major bleeding evolved in patients managed conservatively. No sequelae were documented in 23 (44%) of 52 episodes of phytonadione (vitamin K1) administration. Sixteen (31%) episodes of major bleeding were documented, but bleeding occurred before phytonadione administration in all cases. Administering phytonadione resulted in hospital admission for 3 patients: 2 (3.8%) because of thromboembolism and 1 (1.9%) for the administration of heparin sodium. Cost-effectiveness analysis determined that treatment with phytonadione is 7 times more costly than conservative management when INRs are between 6.0 and 10.0.

Conclusions: Most episodes of excessive anticoagulation were not managed per consensus guidelines. The higher the INR, the more likely were interventions to adhere to the guidelines. Administering phytonadione to patients with a moderate elevation of INRs (6.0-10.0) may be unnecessary. Based on this study, conservative management is a viable option.

Prognosis and Treatment of Bile Duct Carcinoma

Chung C; Bautista N; O'Connell TX; Am Surg 1998 Oct;64(10):921-5.

Bile duct carcinomas present a therapeutic challenge because of different histologies, tumor locations, and resectabilities. The goal of our study was to identify prognostic factors to better delineate therapeutic options. Forty patients (30 males and 10 females) diagnosed with bile duct cancer, treated between 1985 and 1996, at Kaiser Permanente Medical Center, Los Angeles were retrospectively reviewed. Three prognostically significant variables were identified: tumor histology, tumor location, and resection. Papillary histology was the most significant determinant of long-term survival. Of six patients with papillary adenocarcinoma, four patients (67%) underwent resection, with all four achieving long-term survival. Lower-third lesions also demonstrated a survival advantage. Four out of 12 (33%) lower-third tumors were resected, with a median survival of 36 months. Irrespective of tumor histology or tumor location, tumor resection always afforded longer survival times than did palliative treatments. A prognostic classification system based on weighted values of significant variables is presented that accurately predicted long-term survival. In con-

clusion, bile duct tumors in general are incurable, except perhaps for a small subset of patients with papillary adenocarcinoma. Papillary histology is the most significant determinant of ultimate survival and cure. A multifunctional prognostic classification system can be helpful for this perplexing disease.

Decline in Incidence of Endometrial Cancer Following Increase in Prescriptions for Opposed Conjugated Estrogens in a Prepaid Health Plan

Ziel HK; Finkle WD; Greenland S; Gynecologic Oncology 1998 Mar;68(3):253-5.

During the 1980s, the ecologic association of conjugated estrogens with endometrial cancer changed from positive to negative in a prepaid health plan. During the same period, use of progestins increased dramatically. We investigated whether the latter increase could explain the reversal of the estrogen-cancer association. Endometrial cancer incidence was estimated from cases recorded in the health plan registry divided by the number of women over age 45 years. Conjugated estrogens usage was measured as milligrams prescribed per woman per year and progestin was measured as tablets per woman per year, both based upon pharmacy records. Graphical and regression methods were used to analyze the resulting ecologic data. In a log-linear regression of incidence on conjugated estrogens and medroxyprogesterone usage, estrogen usage had a strong positive association with incidence, while medroxyprogesterone had a strong negative association with incidence. The change in the direction of the ecologic association between estrogen and endometrial cancer that occurred in 1984 continued until 1993, suggesting that the decline in endometrial cancer incidence and concomitant increase in conjugated estrogens usage since 1984 is explained by the increasing use of progestins. The data are entirely consistent with the hypothesis that progestins can protect against most of the excess risk conferred by conjugated estrogens, although the ecologic nature of the data prohibits drawing further inferences.

Factors Associated with Antibiotic Use for Acute Bronchitis

Gonzales R; Barrett PH Jr.; Crane LA; Steiner JF; J Gen Intern Med 1998 Aug;13(8):541-8.

Objectives: To describe the clinical features of adults diagnosed with acute bronchitis, and to identify clinical variables associated with antibiotic treatment of acute bronchitis.

Design: Prospective, cohort study.

Setting: Primary care office practices at a group-model HMO in the Denver metropolitan area.

Patients/Participants: Patients were adults seeking care for acute respiratory illnesses. Participating clinicians included internists, family medicine physicians, nurse practitioners, physician assistants, and registered nurses.

Measurements and Main Results: Clinicians voluntarily completed encounter forms for patients presenting with acute respiratory illnesses between February and May, 1996. Acute bronchitis was the primary diagnosis in 16% of acute respiratory illness visits (n=1525). The most frequent symptoms of acute bronchitis were cough (92%), phlegm production (63%), "runny nose" (50%), and throat pain (50%). The most frequent physical examination findings were pharyngeal erythema (45%), cervical lymphadenopathy (19%), wheezes (18%), and rhonchi (17%). Antibiotics were prescribed to 85% of patients diagnosed with acute bronchitis. Purulent nasal discharge by patient report, and sinus tenderness on physical examination were moderately associated with antibiotic treatment ($p = .06$ and .08, respectively). Antibiotic prescription rates did not vary by patient age or gender, duration of illness, days of work lost due to illness, or clinician type.

Conclusions: Acute bronchitis is frequently treated with antibiotics in ambulatory practice. The clinical factors we identified to be associated with antibiotic use for acute bronchitis appear to play a minor role in explaining the excessive use of antibiotics for this condition. These findings suggest that clinicians use the diagnosis of acute bronchitis as an indication for antibiotic treatment, despite clinical trials and expert recommendations to the contrary.

Successful Outpatient Management of Acute Upper Gastrointestinal Hemorrhage: Use of Practice Guidelines in a Large Patient Series

Longstreth GF, Feitelberg SP; Gastrointestinal Endoscopy 1998 Mar;47(3):219-22.

Background: Acute upper gastrointestinal hemorrhage is a common reason for hospitalization. Clinical and endoscopic characteristics predict outcome. The aim of this study was to determine the characteristics and outcome of patients with acute upper gastrointestinal hemorrhage cared for without hospitalization.

Methods: One hundred seventy-six consecutive

patients in a staff-model health maintenance organization were selected for outpatient care based on absolute endoscopic and non-absolute clinical criteria. Clinical and endoscopic characteristics, British national audit "risk scores," and rates of recurrent bleeding, hospitalization, and mortality were determined.

Results: Mean patient age (+/-SD) was 56.4 +/- 16.0 years, and 106 patients (60%) were men. One hundred one (57%) had endoscopy within 2 days of the onset of hemorrhage. The mean initial hemoglobin concentration was 11.7 +/- 2.3 mg/dL. Ninety-seven patients (55%) had a peptic ulcer, and 57 (32%) had a British risk score greater than 2. Hospitalization, recurrent bleeding, and mortality occurred in two (1%), one (1%), and zero (0%) patients, respectively, during 16.0 +/- 10.8 months of follow-up.

Conclusions: Many patients with acute upper gastrointestinal hemorrhage can be safely treated as outpatients using endoscopic and clinical guidelines.

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Examination of the Prevalence and Seasonal Variation of Intestinal Microsporidiosis in the Stools of Persons with Chronic Diarrhea and Human Immunodeficiency Virus Infection

Conteas CN; Berlin OG; Lariviere MJ; Pandhumas SS; Speck CE; Porschen R; Nakaya T; Am J Trop Med Hyg 1998 May;58(5):559-61.

The epidemiology of human microsporidiosis is poorly understood and environmental factors affecting transmission of the organism have not been fully elucidated. Temporal variation in the prevalence of microsporidia in the stool of patients with human immunodeficiency virus (HIV) infection and diarrhea was studied to evaluate the role of water-borne transmission. From January 1993 to December 1996, 8439 stools from HIV-infected individuals were examined for microsporidia spores in southern California. Yearly positivity rates were 8.8% in 1993, 9.7% in 1994, 6.6% in 1995, and 2.9% in 1996. An analysis for linear trend showed a statistically significant decrease in stool positivity rates of time (chi2 = 81.9, P = 0.001). No significant seasonal variation in the prevalence of microsporidiosis was seen over that time period. These results suggest the constant presence of microsporidia in the environment, rather than a seasonal association with recreational water use or seasonal contamination of the water supply, and a real decrease in yearly prevalence of microsporidia-related diarrhea. Factors related to a progressive decrease in prevalence are subjects of future investigation.

Declining Cesarean Delivery Rates in California: An Effect of Managed Care?

Weinstein RB; Trussell J.; Am J Obstet and Gynecol 1998 Sep;179(3 Pt 1):657-64.

Objectives: We hypothesized that movement from traditional indemnity insurance to managed care in California between 1983 and 1994 would lead to reductions in the rate of cesarean delivery.

Study Design: We decomposed the frequency of cesarean delivery with each primary diagnosis into the product of the diagnosis rate among all women and the cesarean delivery rate among women with the given diagnosis (conditional cesarean delivery rate). We used logistic regression to estimate the diagnosis and conditional cesarean delivery rates.

Results: Adjusted and observed cesarean delivery rates are indistinguishable. Both the diagnosis rates and the conditional cesarean delivery rates contributed to the increase in the cesarean delivery rate between 1983 and 1987. The subsequent decline is attributable to the decline in the repeated cesarean delivery rate.

Conclusions: The increase in managed care in California played no apparent role in the decline in the cesarean delivery rate. With the exception of Kaiser health maintenance organizations, managed care providers and indemnity insurers managed deliveries similarly.

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Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults. The Adverse Childhood Experiences (ACE) Study

Felitti VJ; Anda RF; Nordenberg D; Williamson DF; Spitz AM; Edwards V; Koss MP; Marks JS; Am J Prev Med 1998 May;14(4):245-58.

Background: The relationship of health risk behavior and disease in adulthood to the breadth of exposure to childhood emotional, physical, or sexual abuse, and household dysfunction during childhood has not previously been described.

Methods: A questionnaire about adverse childhood experiences was mailed to 13,494 adults who had completed a standardized medical evaluation at a large HMO; 9,508 (70.5%) responded. Seven categories of adverse childhood experiences were studied: psychological, physical or sexual abuse; violence against mother; or living with household members who were substance abusers, mentally ill or suicidal, or ever imprisoned. The number of categories of these adverse childhood experiences was then compared to measures of adult risk behavior, health status, and disease. Logistic regression was used

to adjust for effects of demographic factors on the association between the cumulative number of categories of childhood exposures (range: 0-7) and risk factors for the leading causes of death in adult life.

Results: More than half of respondents reported at least one, and one-fourth reported ≥2 categories of childhood exposures. We found a graded relationship between the number of categories of childhood exposure and each of the adult health risk behaviors and diseases that were studied (P< .001). Persons who had experienced four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold increased health risks for alcoholism, drug abuse, depression, and suicide attempt; a 2- to 4-fold increase in smoking, poor self-rated health, ≥50 sexual intercourse partners, and sexually transmitted disease; and a 1.4 to 1.6-fold increase in physical inactivity and severe obesity. The number of categories of adverse childhood exposures showed a graded relationship to the presence of adult diseases including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. The seven categories of adverse childhood experiences were strongly interrelated and persons with multiple categories of childhood exposure were likely to have multiple health risk factors later in life.

Conclusions: We found a strong graded relationship between the breadth of exposure to abuse or household dysfunction during childhood and multiple risk factors for several of the leading causes of death in adults.

Marijuana Use and Medically Attended Injury Events

Braun BL; Tekawa IS; Gerberich SG; Sidney S; Ann Emerg Med 1998 Sep;32(3 Pt 1):353-60.

Study Objective: This study evaluated the relation between self-reported marijuana use and 3-year incidence of injury.

Methods: We conducted a retrospective cohort study of adult Kaiser Permanente Medical Care Program members who underwent multiphasic health examinations between 1979 and 1986 (n=4462). Injury-related outpatient visits, hospitalizations, and fatalities within 3 years of examination were determined.

Results: Outpatient injury events totaled 2524; 1611 participants (36%) had at least 1 injury-related outpatient visit. Injury-related hospitalizations (n=22) and fatalities (n=3) were rare. Among men, there was no consistent relation between marijuana use and injury incidence for either former users (rate ratio, 1.15; 95% confidence interval [CI], .97 to 1.36) or current users (rate ratio, 0.97; 95% CI, .81 to 1.17), compared with those who had never used marijuana. Among women, former and current users showed little difference in their rate of later injury compared with never users; the rate ratios were 1.05 (95% CI, .87 to 1.26) and 1.20 (95% CI, 1.00 to 1.44), respectively. No statistically significant associations were noted between marijuana use and cause-specific injury incidence in men or women.

Conclusion: Among members of a health maintenance organization, self-reported marijuana use in adult men or women was not associated with outpatient injury within 3 years of marijuana use ascertainment.

Nurses' and Pharmacists' Exposure to Antineoplastic Drugs: Findings from Industrial Hygiene Scans and Urine Mutagenicity Tests

Labuhn K, Valanis B, Schoeny R, Loveday K, Vollmer WM; Cancer Nurs 1998 Apr;21(2):79-89.

Data from 83 nurses and pharmacists handling antineoplastic drugs and 35 nurse/pharmacist controls who participated in a national study of antineoplastic drug-handling risks were examined to investigate antineoplastic drug exposure. Measures of external exposure included self-completion drug logs and industrial hygiene scans conducted in clinical settings. Internal exposure was measured by urine mutagenicity tests on end-of-week 24-hour urine specimens. To control for potential confounders, the staff was asked to complete food and hobby diaries and to avoid identified mutagenic substances for one week before collection of 24-hour urine samples. On the scans of the drug handlers, 13% showed one or more spots of drug contamination on gloved and ungloved hands, gowns, or shoes. Of the 24-hour urine samples, 15% were mutagenic for Salmonella typhimurium: Rates did not differ significantly for drug handlers and controls. Among nurses who both prepared and administered antineoplastics, those with positive mutagenicity tests handled more doses of the drugs, used less skin protection, and had more skin contact with the drugs than those with negative tests. Nurses who only administered the drugs and had positive mutagenicity tests handled fewer doses of drugs than those with negative tests, but they also reported less use of protection and more skin contact. For both groups of nurses, skin contact with antineoplastics was associated with positive mutagenicity test results ($p < 0.01$). ❖