abstract of
New England Journal of Medicine

Volume 356, Number 13 & 14 - 29 March & 5 April, 2007
table of contents

PERSPECTIVES

The demise of the blockbuster?
Cutler, D.M

Benefits with risks: Bush’s tax-based health care proposals
Reischauer, R.D

Making motherhood safe in developing countries
Rosenfield, A., Caroline J. Min, and Lynn P. Freedman

The egg trade: making sense of the market for human oocytes
Spar, D.

ORIGINAL ARTICLES

Telomerase mutations in families with idiopathic pulmonary fibrosis

Asthma control during the year after bronchial thermoplasty

Vitamins and perinatal killer T cells in asthma and chronic obstructive pulmonary disease
Fawzi, W.W., Germond I. Msamanga, Willy Urassa, Ellen Hertzmark, Paul Petrau, Walter C. Willett, and Donna Spiegelman

Influence of Computer-Aided Detection on Performance of Screening Mammography

Brief report: mutations in VANGL1 associated with neural-tube defects
Kibar, Z., Elena Torban, Jonathan R. McDearmid, Annie Reynolds, Joanne Berghout, Melissa Mathieu, Irena Kirillova, Patrizia De Marco, Elisa Merello, Julie M. Hayes, John B. Wallingford, Pierre Drapeau, Valeria Capra

MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer

Effect of torcetrapib on phenotype of coronary atherosclerosis

Invariant Natural Killer T Cells in Asthma and Chronic Obstructive Pulmonary Disease
Vijayanand, P., Chris Pickard, Robert M. Powell, Gilbert Angco, David Sammut, Stephan D. Gadomski, Peter S. Friedmann, and Ratko Djukanovi

CLINICAL THERAPEUTICS

Varicella: zoster vaccine for the prevention of herpes zoster
Kimberlin, D.W., and Richard J. Whitley

Current concepts: withdrawal of albuterol inhalers containing chlorofluorocarbon propellants
Hendeles, L., Gene L. Colice, and Robert J. Meyer

Current concept: viral hepatitis in HIV infection
Koziel, M.J., and Marion G. Peters

IMAGES IN CLINICAL MEDICINE

A medical mystery: skin discolorations in a bank employee
Schanz, S., and G Melzler

Rapid progression of basal-type breast cancer
Seewaldt, V.L., and V. Scott

 Conjunctival viral papillomas
Tulvatana, W., and K. Kulvichit

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Case 10-2007: a 55-year-old man impaled in a rowing accident
Sheridan, R.L., George Velmahos, Malcolm Smith, and Richard Sacknoff

CLINICAL PRACTICE

Prophylaxis for thromboembolism in hospitalized medical patients
Francis, C.W.

CLINICAL PROBLEM-SOLVING

Building a diagnosis from the ground up: A 49-year-old man came to the clinic with a 1-week history of suprapubic pain and fever
Watts, B., Pushkar Argekar, Sanjay Saint, and Carol A. Kauffman
Anna Behrens is 24 years old. Tall and slim, she is working toward her Ph.D. in art history at an Ivy League school. During her undergraduate years, Anna accumulated $27,000 in credit-card debt. In the fall of 2005, frustrated by her economic straits, Anna answered an advertisement in her university’s magazine promising $25,000 to a “tall, athletic woman” willing to “give a gift of life and love.” Anna visited the agent who had placed the ad, underwent medical tests at a fertility clinic, and met the couple that was searching for eggs. Through the agent, they offered her $20,000 plus medical expenses. Six weeks later, after 2 weeks of hormone injections, mood swings, and bloating, Anna returned to the clinic and had eight healthy oocytes removed. The couple took them, and Anna took her money. She will probably never know whether her eggs resulted in a successful pregnancy…

ORIGINAL ARTICLES


Idiopathic pulmonary fibrosis is progressive and often fatal; causes of familial clustering of the disease are unknown. Germline mutations in the genes hTERT and hTR, encoding telomerase reverse transcriptase and telomerase RNA, respectively, cause autosomal dominant dyskeratosis congenita, a rare hereditary disorder associated with premature death from aplastic anemia and pulmonary fibrosis. Methods To test the hypothesis that familial idiopathic pulmonary fibrosis may be caused by short telomeres, we screened 73 probands from the Vanderbilt Familial Pulmonary Fibrosis Registry for mutations in hTERT and hTR. Six probands (8%) had heterozygous mutations in hTERT or hTR; mutant telomerase resulted in short telomeres. Asymptomatic subjects with mutant telomerase also had short telomeres, suggesting that they may be at risk for the disease. We did not identify any of the classic features of dyskeratosis congenita in five of the six families. Mutations in the genes encoding telomerase components can appear as familial idiopathic pulmonary fibrosis. Our findings support the idea that pathways leading to telomere shortening are involved in the pathogenesis of this disease.


Bronchial thermoplasty is a bronchoscopic procedure to reduce the mass of airway smooth muscle and attenuate bronchoconstriction. We examined the effect of bronchial thermoplasty on the control of moderate or severe persistent asthma. We randomly assigned 112 subjects who had been treated with inhaled corticosteroids and long-acting adrenergic agonists (LABA) and in whom asthma control was impaired when the LABA were withdrawn to either bronchial thermoplasty or a control group. The primary outcome was the frequency of mild exacerbations, calculated during three
scheduled 2-week periods of abstinence from LABA at 3, 6, and 12 months. Airflow, airway responsiveness, asthma symptoms, the number of symptom-free days, use of rescue medication, and scores on the Asthma Quality of Life Questionnaire (AQLQ) and the Asthma Control Questionnaire (ACQ) were also assessed. The mean rate of mild exacerbations, as compared with baseline, was reduced in the bronchialthermoplasty group but was unchanged in the control group (change in frequency per subject per week, 0.16±0.37 vs. 0.04±0.29; P<0.005). At 12 months, there were significantly greater improvements in the bronchialthermoplasty group than in the control group in the morning peak expiratory flow (39.3±48.7 vs. 8.5±44.2 liters per minute), scores on the AQLQ (1.3±1.0 vs. 0.6±1.1) and ACQ (reduction, 1.2±1.0 vs. 0.5±1.0), the percentage of symptom-free days (40.6±39.7 vs. 17.0±37.9), and symptom scores (reduction, 1.9±2.1 vs. 0.7±2.5) while fewer puffs of rescue medication were required. Values for airway responsiveness and forced expiratory volume in 1 second did not differ significantly between the two groups. Adverse events immediately after treatment were more common in the bronchialthermoplasty group than in the control group but were similar during the period from 6 weeks to 12 months after treatment. Bronchial thermoplasty in subjects with moderate or severe asthma results in an improvement in asthma control.


Prematurity and low birth weight are associated with high perinatal and infant mortality, especially in developing countries. Maternal micronutrient deficiencies may contribute to these adverse outcomes. In a double-blind trial in Dar es Salaam, Tanzania, we randomly assigned 8468 pregnant women (gestational age of fetus, 12 to 27 weeks) who were negative for human immunodeficiency virus infection to receive daily multivitamins (including multiples of the recommended dietary allowance) or placebo. All the women received prenatal supplemental iron and folic acid. The primary outcomes were low birth weight (<2500 g), prematurity, and fetal death. The incidence of low birth weight was 7.8% among the infants in the multivitamin group and 9.4% among those in the placebo group (relative risk, 0.82; 95% confidence interval [CI], 0.70 to 0.95; P<0.01). The mean difference in birth weight between the groups was modest (67 g, P<0.001). The rates of prematurity were 16.9% in the multivitamin group and 16.7% in the placebo group (relative risk, 1.01; 95% CI, 0.91 to 1.11; P=0.87), and the rates of fetal death were 4.3% and 5.0%, respectively (relative risk, 0.87; 95% CI, 0.72 to 1.05; P=0.15). Supplementation reduced both the risk of a birth size that was small for gestational age (<10th percentile; 10.7% in the multivitamin group vs. 13.6% in the placebo group; relative risk, 0.77; 95% CI, 0.68 to 0.87; P<0.001) and the risk of maternal anemia (hemoglobin level, <11 g per deciliter; relative risk, 0.88; 95% CI, 0.80 to 0.97; P<0.01), although the difference in the mean hemoglobin levels between the groups was small (0.2 g per deciliter, P=0.001). Multivitamin supplementation reduced the incidence of low birth weight and small-for-gestational-age births but had no significant effects on prematurity or fetal death. Multivitamins should be considered for all pregnant women in developing countries.


Computer-aided detection identifies suspicious findings on mammograms to assist radiologists. Since the Food and Drug Administration approved the technology in 1998, it has been disseminated into practice, but its effect on the accuracy of interpretation is unclear. We determined the association between the use of computer-aided detection at mammography facilities and the performance of screening mammography from 1998 through 2002 at 43 facilities in three states. We had complete data for 222,135 women (a total of 429,345 mammograms), including 2351 women who received a diagnosis of breast cancer within 1 year after screening. We calculated the specificity, sensitivity, and positive predictive value of screening mammography with and without computer-aided detection, as well as the rates of biopsy and breast-cancer detection and the overall accuracy, measured as the area under the receiver-operating-characteristic (ROC) curve. Seven facilities (16%) implemented computer-aided detection during the study period. Diagnostic specificity decreased from 90.2% before implementation to 87.2% after implementation (P<0.001), the positive predictive value decreased from 4.1% to 3.2% (P=0.01), and the rate of biopsy increased by 19.7% (P<0.001). The increase in sensitivity from 80.4% before implementation of computer-aided detection to 84.0% after implementation was not significant (P=0.32). The change in the cancer-detection rate (including invasive breast cancers and ductal carcinomas in situ) was not significant (4.15 cases per 1000 screening mammograms before implementation and 4.20 cases after implementation, P=0.90). Analyses of data from all 43 facilities showed that the use of computer-aided detection was associated with significantly lower overall accuracy than was nonuse (area under the ROC curve, 0.871 vs. 0.919; P=0.005). The use of computer-aided detection is associated with reduced accuracy of interpretation of screening mammograms. The increased rate of biopsy with the use of computer-aided detection is not clearly associated with improved detection of invasive breast cancer.


Neural-tube defects such as anencephaly and spina bifida constitute a group of common congenital malformations caused by complex genetic and environmental factors. We
have identified three mutations in the VANGL1 gene in patients with familial types (V239I and R274Q) and a sporadic type (M328T) of the disease, including a spontaneous mutation (V239I) appearing in a familial setting. In a protein–protein interaction assay V239I abolished interaction of VANGL1 protein with its binding partners, disheveled-1, -2, and -3. These findings implicate VANGL1 as a risk factor in human neural-tube defects.


Even after careful clinical and mammographic evaluation, cancer is found in the contralateral breast in up to 10% of women who have received treatment for unilateral breast cancer. We conducted a study to determine whether magnetic resonance imaging (MRI) could improve on clinical breast examination and mammography in detecting contralateral breast cancer soon after the initial diagnosis of unilateral breast cancer. A total of 969 women with a recent diagnosis of unilateral breast cancer and no abnormalities on mammographic and clinical examination of the contralateral breast underwent breast MRI. The diagnosis of MRI-detected cancer was confirmed by means of biopsy within 12 months after study entry. The absence of breast cancer was determined by means of biopsy, the absence of positive findings on repeat imaging and clinical examination, or both at 1 year of follow-up. MRI detected clinically and mammographically occult breast cancer in the contralateral breast in 30 of 969 women who were enrolled in the study (3.1%). The sensitivity of MRI in the contralateral breast was 91%, and the specificity was 88%. The negative predictive value of MRI was 99%. A biopsy was performed on the basis of a positive MRI finding in 121 of the 969 women (12.5%), 30 of whom had specimens that were positive for cancer (24.8%); 18 of the 30 specimens were positive for invasive cancer. The mean diameter of the invasive tumors detected was 10.9 mm. The additional number of cancers detected was not influenced by breast density, menopausal status, or the histologic features of the primary tumor.


Levels of high-density lipoprotein (HDL) cholesterol are inversely related to cardiovascular risk. Torcetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, increases HDL cholesterol levels, but the functional effects associated with this mechanism remain uncertain. A total of 1188 patients with coronary disease underwent intravascular ultrasonography. After treatment with atorvastatin to reduce levels of low-density lipoprotein (LDL) cholesterol to less than 100 mg per deciliter (2.59 mmol per liter), patients were randomly assigned to receive either atorvastatin monotherapy or atorvastatin plus 60 mg of torcetrapib daily. After 24 months, disease progression was measured by repeated intravascular ultrasonography in 910 patients (77%). After 24 months, as compared with atorvastatin monotherapy, the effect of torcetrapib–atorvastatin therapy was an approximate 61% relative increase in HDL cholesterol and a 20% relative decrease in LDL cholesterol, reaching a ratio of LDL cholesterol to HDL cholesterol of less than 1.0. Torcetrapib was also associated with an increase in systolic blood pressure of 4.6 mm Hg. The percent atheroma volume (the primary efficacy measure) increased by 0.19% in the atorvastatin-only group and by 0.12% in the torcetrapib–atorvastatin group (P=0.72). A secondary measure, the change in normalized atheroma volume, showed a small favorable effect for torcetrapib (P=0.02), but there was no significant difference in the change in atheroma volume for the most diseased vessel segment. The CETP inhibitor torcetrapib was associated with a substantial increase in HDL cholesterol and decrease in LDL cholesterol. It was also associated with an increase in blood pressure, and there was no significant decrease in the progression of coronary atherosclerosis. The lack of efficacy may be related to the mechanism of action of this drug class or to molecule-specific adverse effects.


The number of type 2 helper CD4+ T cells is increased in the airways of persons with asthma. Whether the majority of these cells are class II major-histocompatibility-complex–restricted cells or are among the recently identified CD1d-restricted invariant natural killer T cells is a matter of controversy. We studied the frequency of invariant natural killer T cells in the airways of subjects with mild or moderately severe asthma to investigate the possibility of an association between the number of invariant natural killer T cells in the airway and disease severity. We also studied whether an increased number of these cells is a feature of chronic obstructive pulmonary disease (COPD). We enumerated invariant natural killer T cells by flow cytometry with the use of CD1d tetramers loaded withgalactosylceramide and antibodies specific to the invariant natural killer T-cell receptor in samples of bronchoalveolar-lavage fluid, induced sputum, and bronchial-biopsy specimens obtained from subjects with mild or moderately severe asthma, subjects with COPD, and healthy control subjects. Real-time polymerase-chain-reaction analysis was performed on bronchoalveolar-lavage cells for evidence of gene expression of the invariant natural killer T-cell receptor. Fewer than 2% of the T cells obtained from all subjects on airway biopsy, bronchoalveolar lavage, and sputum induction were invariant natural killer T cells, with no significant differences among the three groups of subjects. No expression of messenger RNA for the invariant natural killer T-cell–receptor was detected in bronchoalveolar-lavage cells from subjects with asthma.
Invariant natural killer T cells are found in low numbers in the airways of subjects with asthma, subjects with COPD, and controls.

**CLINICAL THERAPEUTIC**
*(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)*


Albuterol (called salbutamol outside the United States) is delivered by a metered-dose inhaler, the most widely used drug and delivery method in this class of agents worldwide. In the United States, about 52 million prescriptions for albuterol are filled annually, mostly as generic products containing chlorofluorocarbon (CFC) propellants, making it the seventh most commonly prescribed medication in...


Hepatitis C virus (HCV) and hepatitis B virus (HBV) infections are common among patients with human immunodeficiency virus (HIV) infection because of shared routes of viral transmission. Liver disease due to chronic HBV and HCV infection is becoming a leading cause of death among persons with HIV infection worldwide, and the risk of death related to liver disease is inversely related to the CD4 cell count...

**IMAGES IN CLINICAL MEDICINE**
*(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)*


A healthy 34-year-old female bank employee presented with black discolorations of the skin on all her fingers. The discolorations had developed in the evening, after work. She was unable to remove the spots, even with the use of various abrasives. She had no other acute symptoms. The same symptoms had developed in some of her colleagues. What is the diagnosis?


A 33-year-old woman with a known BRCA1 mutation (2080delA) was referred for 3.0-tesla magnetic resonance imaging (3T MRI). The patient’s mother had had breast cancer at the ages of 31 and 38 years; her sister had had breast cancer at the age of 30. Routine physical examination revealed no breast masses, and screening mammography showed extreme breast density but was otherwise normal. At follow-up approximately 4 months later, 3T MRI showed a progressively enhancing lesion, 1.6 by 1.0 cm (Panel A, arrow). Mammographic imaging showed new calcifications at the 10 o’clock position. A stereotactic biopsy was performed; 4 of 10 cores showed calcifications, and all cores showed ductal hyperplasia with no evidence of cancer. Approximately 1 year later, repeated 3T MRI showed a peripherally...

**REVIEW ARTICLES**
*(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)*


This Journal feature begins with a case vignette that includes a therapeutic recommendation. A discussion of the clinical problem and the mechanism of benefit of this form of therapy follows. Major clinical studies, the clinical use of this therapy, and potential adverse effects are reviewed. Relevant formal guidelines, if they exist, are presented. The article ends with the authors’ clinical recommendations.


A healthy 9-year-old boy had a 1-year history of an itchy right eye with frequent tearing. Small masses that gradually developed in the right caruncula lacrimalis area were associated with intermittent, spontaneous minor bleeding. The ophthalmic examination showed diffuse, multifocal small nodules with papillomatous growth and vascular fronds. The upper and lower tarsal conjunctiva was also involved (Panel A). No warts were noted on the remainder of the physical examination. A histopathological examination of the ocular lesion revealed acanthotic conjunctival epithelial growth in a fingerlike pattern with central fibrovascular cores (Panel B). Koilocytosis, a nuclear pyknosis with cytoplasmic clearing, was...

**CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL**
*(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)*


A 55-year-old man was admitted to this hospital after being impaled by the prow of a racing shell in a rowing accident. The patient, who was in excellent health, was sculling on the Charles River in Boston when his boat collided head-on at approximately 7:20 a.m. with an eight-person shell moving in the opposite direction; both boats were estimated to be traveling at 24 to 32 km per hour. The initial contact between the vessels tore a rubber safety bumper from the larger boat, and the sharp prow of the larger craft entered the left side of...
the patient’s lower . . .

CLINICAL PRACTICE
(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)


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 62-year-old man is admitted with fever, cough, and dyspnea. He is weak, appears to be dehydrated, and has purulent sputum. His temperature is 39.2°C, respirations 22, and blood pressure 128/69 mm Hg. There are crackles over the left lower lung field, and chest radiography shows a density in the left lower lobe that is consistent with . . .

CLINICAL PROBLEM-SOLVING
(Since these articles has no abstract, we just provided an extract of the first 100 words of the full text and any section headings)


In this Journal feature, information about a real patient is presented in stages (boldface type) to an expert clinician, who responds to the information, sharing his or her reasoning with the reader (regular type). The authors’ commentary follows. A 49-year-old man came to the clinic with a 1-week history of suprapubic pain and fever. On examination, he had a temperature of 38.1°C but appeared well. A urinalysis revealed numerous white cells, two red cells, and more than two bacteria per high-power field. A urinary tract infection was diagnosed, and oral gatifloxacin was prescribed. Possible causes of this patient’s illness include . . .