Elevated parathyroid hormone 44-68 and osteoarticular changes in patients with genetic hemochromatosis.

Arthritis & Rheumatism. 42(4):799-806, 1999 Apr.

OBJECTIVE: To determine whether the osteoarticular changes associated with genetic hemochromatosis could be explained by metabolic parathyroid hormone (PTH) disorders.

METHODS: The study involved 210 patients with liver iron overload syndromes. Osteoarticular changes were numerically scored as the number of damaged joints. PTH 1-84 and 44-68 were assayed.

RESULTS: An increase in serum PTH 44-68 levels was found in one-third of untreated patients who had no calcium or PTH 1-84 abnormalities. Serum PTH 44-68 levels correlated positively with serum ferritin levels. In MULTIVARIATE analyses, the number of affected joints correlated positively with age, serum PTH 44-68 levels, and serum ferritin levels.

CONCLUSION: Liver iron overload syndromes, especially genetic hemochromatosis, are associated with elevated circulating levels of PTH fragments containing the 44-68 region, which appears to play a role in osteoarticular changes. This increase seems to be a consequence of iron overload.

Pneumocystis carinii pneumonia in patients with connective tissue diseases: the role of hospital experience in diagnosis and mortality.Arthritis & Rheumatism. 42(4):780-9, 1999 Apr.

OBJECTIVE: Pneumonia due to Pneumocystis carinii has been increasingly reported in patients with connective tissue diseases, but the frequency of this complication is not known. We sought to determine the frequency of P carinii pneumonia (PCP) in patients with connective tissue diseases, and to determine the role that a hospital's acquired immunodeficiency syndrome (AIDS)-related experience may have in the diagnosis of PCP in these patients. METHODS: We used a state hospitalization registry to identify all patients with PCP and either rheumatoid arthritis, systemic lupus erythematosus, Wegener's granulomatosis, polymyositis, dermatomyositis, polyarteritis nodosa, or scleroderma who had an emergent or urgent hospitalization in California from 1983 to 1994. We compared patient and hospital characteristics between these patients and patients with connective tissue diseases hospitalized with other types of pneumonia. RESULTS: Two hundred twenty-three patients with connective tissue diseases were diagnosed with PCP in the 12-year study period. The frequency of PCP ranged from 89 cases/10,000 hospitalizations/year in patients with Wegener's granulomatosis to 2 cases/10,000 hospitalizations/year in patients with rheumatoid arthritis. Compared with 5,457 patients with connective tissue diseases and pneumonia due to other organisms, patients with PCP were more likely to be younger, to be male, to have private medical insurance, and to have systemic lupus erythematosus, Wegener's granulomatosis, inflammatory myopathy, or polyarteritis nodosa rather than rheumatoid arthritis, and were less likely to be African American. Hospital size, teaching status, urban/rural location, proportion of admissions due to AIDS or PCP, and proportion of patients with pneumonia undergoing bronchoscopy were each associated with the likelihood of diagnosis of PCP in univariate analyses, but only the number of patients with PCP being treated at a hospital (odds ratio [OR] 1.03 for each additional 10 cases/year, 95% confidence interval [95% CI] 1.01-1.05) was associated with the likelihood of diagnosis of PCP in MULTIVARIATE analyses. Patients were also somewhat more likely to be diagnosed with PCP if there had previously been a case of PCP in a patient with a connective tissue disease at the same hospital (OR 135, 95% CI 0.98-1.85). In-hospital mortality was 45.7%, and was unrelated to hospital characteristics. CONCLUSION: PCP is an uncommon, but often fatal, occurrence in patients with connective tissue disease. A hospital's prior experience with patients with PCP is associated with the likelihood that this condition is diagnosed in patients with connective tissue diseases who present with pneumonia, suggesting that diagnostic suspicion is an important factor in the correct identification of affected patients.

Emotional and behavioural problems and competencies among immigrant and non-immigrant adolescents. Australian & New Zealand Journal of Psychiatry. 32(5):658-65, 1998 Oct.

OBJECTIVE: The aim of this study was to compare levels of emotional and behavioural problems and competencies among immigrant and non-immigrant adolescents, and to determine factors that may contribute to any differences reported.

METHOD: Subjects were selected randomly from students aged 12-16 years attending a high school with a high proportion of immigrants in Perth, Western Australia. Parents completed the Child Behaviour Checklist (CBCL), and students completed the Youth Self-Report (YSR) and a Personal History Questionnaire.

RESULTS: On univariate analyses, non-immigrant adolescents had significantly higher CBCL and YSR scores than immigrant adolescents. **MULTIVARIATE** analyses suggested that CBCL scores were predicted by a number of variables other than immigration, including family intactness, socioeconomic status (SES) and gender. Higher YSR scores were predicted by non-intact families, school setting and non-immigrant status, and higher competencies scores were predicted by higher SES and parents not being immigrants.

CONCLUSIONS: In assessing the effects of immigration on adolescent mental health, it is important to control for factors associated with adolescent behavioural and emotional problems and to use multiple informants. Overall, immigrant adolescents report fewer total and externalizing problems and fewer competencies than native-born adolescents. This finding may reflect strict immigration policies or cultural differences in definitions of psychopathology and the social expectations for adolescents' behaviour.

Physical Symptoms Distress Index: a sensitive tool to evaluate the impact of pharmacological agents on quality of life. Archives of Internal Medicine. 159(7):693-700, 1999 Apr12.

OBJECTIVES: To examine whether the degree of stress associated with adverse physical side effects correlates with overall quality of life (QOL) and compliance rates. To determine if instruments used to assess QOL can detect differences between treatments that have no known central nervous system effects.

PATIENTS AND METHODS: This randomized, double-blind, parallel group study evaluated 180 to 480 mg of controlled onset, extended release (COER)-verapamil (n = 259) or 30 to 120 mg/d of nifedipine gastrointestinal therapeutic system (GITS) (n = 269) in men and women between 21 and 80 years of age with stages 1 to 3 hypertension. A battery of questions evaluating psychological well-being and a physical symptom distress index was administered after a 4-week placebo washout (baseline) and after 10 weeks of treatment or at dropout.

RESULTS: Both treatments effectively lowered blood pressure, and there were no significant between-group differences in psychosocial QOL. A difference in the level of physical symptom distress was detected between treatments (P = .002; **MULTIVARIATE** analysis of variance), with 7 significant univariate treatment effects, all favoring COER-verapamil, being noted-pedal edema, polyuria, rapid heart beat or palpitations, hives, muscle cramps, abdominal cramps, and headaches. Constipation-related distress increased significantly (P = .001) but to a similar extent with both treatments. The difference in symptom distress tended to predict compliance as there were more withdrawals in the nifedipine GITS group (n = 85) vs COER-verapamil group (n = 64) (P = .08).

CONCLUSIONS: Patient-assessed physical symptom distress is a sensitive, simple technique to evaluate the effect of antihypertensive medications on QOL and tolerability, as shown by its ability to detect the improvement associated with COER-verapamil. Depending on the agents involved, the Physical Symptom Distress Index may more closely predict dropout rates than the traditional psychosocial instruments, as suggested by the lower dropout rate in the COER-verapamil group. Thus, in studying treatment effects on QOL, both the distress of physical symptoms and the impact of psychosocial factors should be evaluated.

Subjective versus statistical model assessment of mortality risk in open heart surgical procedures.

Annals of Thoracic Surgery. 67(3):635-40, 1999 Mar.

BACKGROUND: The aim of this study was to compare the predictive accuracy for open heart surgical mortality between a statistical model based on collection of clinical data and surgeons' subjective risk assessment.

METHODS:Predictive discrimination of both risk assessments (surgeons' and model) was compared through the area under the receiver operating characteristic curve. Logistic regression analysis was used to assess the relation between surgeons' and model predictions to actual outcomes. Calibration of the subjective estimates was evaluated with a chi2 test.

RESULTS: Overall, the area under the receiver operating characteristic curve was 0.76 for the statistical model and 0.70 for the subjective assessment. Logistic regression analysis showed that the statistical model remained significant after accounting for the subjective assessment. Calibration of subjective mortality predictions was poor.

CONCLUSIONS: Surgeons' risk assessment tends to cluster in the middle ranges of risk. Subjective assessment seems accurate in identifying the two extremes of risk but is inaccurate for intermediate risk levels. A **MULTIVARIATE** statistical model improves the accuracy of subjective predictions.

Underuse and overuse of diagnostic testing for coronary artery disease in patients presenting with new-onset chest pain [see comments].
American Journal of Medicine. 106(4):391-8, 1999 Apr.

PURPOSE: To determine the extent of overuse and underuse of diagnostic testing for coronary artery disease and whether the socioeconomic status, health insurance, gender, and race/ethnicity of a patient influences the use of diagnostic tests.

SUBJECTS AND METHODS: We identified patients who presented with new-onset chest pain not due to myocardial infarction at one of five Los Angeles-area hospital emergency departments between October 1994 and April 1996. Explicit criteria for diagnostic testing were developed using the RAND/University of California, Los Angeles, expert panel method. They were applied to data collected by medical record review and patient questionnaire.

RESULTS: Of the 356 patients, 181 met necessity criteria for diagnostic cardiac testing. Of these, 40 (22%) failed to receive necessary tests. Only 7 (3%) of the 215 patients who received some form of cardiac testing had tests that were judged to be inappropriate. Underuse was significantly more common in patients with only a high school education (30% vs 15% for those with some college, P = 0.02) and those without health insurance (34% vs 15% of insured patients, P = 0.01). In a **MULTIVARIATE** logistic regression model, only the lack of a post-high school education was a significant predictor of underuse (odds ratio 2.2, 95% confidence interval 1.0 to 4.4).

CONCLUSION: Among patients with new-onset chest pain, underuse of diagnostic testing for coronary artery disease was much more common than overuse. Underuse was primarily associated with lower levels of patient education.

Inferences on the kinetics of asbestos deposition and clearance among chrysotile miners and millers. American J Industrial Medicine. 35(4):401-12, 1999 Apr.

BACKGROUND: The health effects of asbestos are intimately related to the fate of inhaled fibers in the lungs. The kinetics of asbestos fibers have been studied primarily in rodents. The objective of this study was to explore the application of these kinetic models to human autopsy data.

METHODS: We analyzed the asbestos fiber content of the lungs of 72 Quebec chrysotile miners and millers and 49 control subjects using analytical transmission electron microscopy. Statistical methods included standard **MULTIVARIATE** linear regression and locally weighted regression methods.

RESULTS: The lung burdens of asbestos bodies and chrysotile and tremolite fibers were correlated, as were the concentrations of short, medium, and long fibers of each asbestos variety. There were significant associations between the duration of occupational exposure and the burdens of chrysotile and tremolite. The concentration of chrysotile decreased with the time since last exposure but the concentration of tremolite did not. The clearance rate varied inversely with the length of chrysotile fibers. For fibers greater than 10 mu in length the clearance half-time was estimated to be 8 years.

CONCLUSIONS: The patterns in our data are compatible with both of the hypotheses suggested from rodent experiments; the existence of a long-term sequestration compartment and overload of clearance mechanisms in this compartment.

Cotton dust and endotoxin exposure and long-term decline in lung function: results of a longitudinal study. American Journal of Industrial Medicine. 35(4):321-31, 1999 Apr.

BACKGROUND: To evaluate the relationship between long-term exposure to cotton dust and Gram-negative bacterial endotoxin on lung function, we conducted an 11-year follow-up study of cotton textile workers in Shanghai, China.

METHODS: Workers at a nearby silk-thread manufacturing mill were used as a referent population. Ninety percent of the original cohort of 445 cotton and 467 silk textile workers--both active and retired-- were identified for testing in the 11th year. Questionnaires and spirometric testing were performed, as well as cotton dust and endotoxin sampling at three points over the 11-year follow-up period: at baseline, at Year 5, and at Year 11. After excluding deaths and subjects on sick-leave, 84% of the original cohort had complete health and environmental data.

RESULTS: The data were reanalyzed using generalized estimating equations feedback model which allow for subject transfer over time between work areas, various exposure levels to dust and endotoxin, and FEV1. Cotton workers had a larger loss of FEV1 during the first 5 years of study (-40 mls/yr) as compared with the second 6 years of follow-up (-18 mls/yr). During the same periods, the average decline among silk workers was slightly higher in the first period, but was more consistent (-30 mls/yr vs. -27 mls/yr), and these differences could not be explained by worker selection or dropout. When cumulative exposure to dust and endotoxin were estimated and used in a **MULTIVARIATE** model (GEE) for FEV1 loss, cumulative dust, but not endotoxin, was associated with 11-year loss in FEV1 after adjustments for confounders. There was evidence of feedback between dust-exposure levels and FEV1, indicating the existence of a healthy-worker survivor effect. After accounting for a healthy-worker survivor effect, we found a significant relationship between dust exposure and FEV1 decline.

CONCLUSIONS: Our results suggest that cotton dust is more strongly associated with chronic airflow limitation than associated endotoxins. Further work is needed to clarify potential reversibility after cessation of exposure, and the relative contributions of dust, endotoxin, and tobacco to chronic respiratory impairment in cotton and other vegetable-exposed workers.

Resting heart rate is a risk factor for cardiovascular and noncardiovascular mortality: the Chicago Heart Association Detection Project in Industry. American Journal of Epidemiology. 149(9):853-62, 1999 May 1.

In a prospective cohort study, associations of resting heart rate with risk of coronary, cardiovascular disease, cancer, and all-cause mortality in age-specific cohorts of black and white men and women were examined over 22 years of follow-up.

Participants were employees from 84 companies and organizations in the Chicago, Illinois, area who volunteered for a screening examination. Participants included 9,706 men aged 18-39 years, 7,760 men aged 40-59 years, 1,321 men aged 60-74 years, 6,928 women aged 18-39 years, 6,915 women aged 40-59 years, and 1,151 women aged 60-74 years at the baseline examination in 1967-1973. Vital status was ascertained through 1992.

For fatal coronary disease, **MULTIVARIATE** -adjusted relative risks associated with a 12 beats per minute higher heart rate (one standard deviation) were as follows: for men aged 18-39 years, relative risk (RR) = 1.27 (95% confidence interval (CI) 1.08-1.48); for men aged 40-59 years, RR = 1.13 (95% CI 1.05-1.21); for men aged 60-74 years, RR = 1.00 (95% CI 0.89-1.12); for women aged 40-59 years, RR = 1.21 (95% CI 1.07-1.36); and for women aged 60-74 years, RR = 1.16 (95% CI 0.99-1.37). Corresponding risks for all fatal cardiovascular diseases were similar to those for coronary death alone. Deaths from cancer were significantly associated with heart rate in men and women aged 40-59 years. All-cause mortality was associated with higher heart rate in men aged 18-39 years (RR = 1.11, 95% CI 1.01-1.20), men aged 40-59 years (RR = 1.16, 95% CI 1.11-1.21), and women aged 40-59 years (RR = 1.20, 95% CI 1.13-1.27). Heart rate was not associated with mortality in women aged 18-39 years.

In summary, heart rate was a risk factor for mortality from coronary disease, all cardiovascular diseases, and all causes in younger men and in middle-aged men and women, and for cancer mortality in middle-aged men and women.

E-cadherin expression as a marker of tumor aggressiveness in routinely processed radical prostatectomy specimens. Urology. 53(4):707-13, 1999 Apr.
OBJECTIVES: Approximately 30% of clinically localized prostate adenocarcinomas treated by radical prostatectomy (RP) will recur within 10 years. To prevent recurrence, new adjuvant therapies are in development that seek to treat high-risk patients after surgery. To identify patients as candidates for these treatments, improved biomarkers for predicting prognosis are needed. Reduced expression of E-cadherin has been proposed as a new marker for predicting prognosis in prostate adenocarcinoma. Since few studies have examined the relation between risk factors for disease progression and E-cadherin expression using routinely processed RP specimens, we used RP specimens to correlate downregulation of E-cadherin and pathologic stage at RP.
METHODS: Primary adenocarcinomas (n = 76) from formalin-fixed and paraffin-embedded RP specimens were evaluated by immunohistochemistry against E-cadherin (HECD-1) using heat-induced epitope retrieval and automated staining (BioTek Solutions). Normal appearing prostate epithelium was used as an internal control for each specimen. Staining was scored as an estimate of the percentage of tumor cells in each specimen that showed strong plasma membrane staining. RESULTS: Specimens were divided into three categories with respect to Gleason score: intermediate (score 5 to 6, n = 31), intermediate to high (score 7, n = 25), and high (score 8 to 9, n = 20). For pathologic stage, specimens were divided into three categories: low stage/organ confined (pT2, n = 30), intermediate stage/limited extraprostatic extension (pT3a, n = 25), and high stage/seminal vesicle-pelvic lymph node metastases (pT3b-any pTN1, n = 21). In univariate analysis, reduced levels of E-cadherin correlated with advanced Gleason score (P = 0.003) and advanced pathologic stage (P = 0.008). In **MULTIVARIATE** analysis, E-cadherin, preoperative prostate-specific antigen, and Gleason score all contributed independently to the prediction of high-stage disease (P<0.0001). Ten pelvic lymph node metastases from this same patient cohort were stained for E-cadherin. All were positive and 9 of 10 were moderately to strongly positive.
CONCLUSIONS: Since essentially all patients in the high-stage category have a very high likelihood of disease recurrence, we conclude that the study of E-cadherin in a prospective manner as a potential biomarker of disease progression in patients with clinically organ-confined prostate cancer who undergo RP is warranted. Additionally, our finding that most metastatic tumor cells in pelvic lymph nodes express E-cadherin supports the notion that the establishment of the distant colonization and growth of metastatic tumor cells may be facilitated by expression or re-expression of previously downregulated E-cadherin. This would strongly suggest that irreversible genetic inactivation through mutation or allelic loss at 16q2.3 is probably not the mechanism of E-cadherin downregulation in most abnormally expressing primary prostate carcinomas.

Lack of a regular source of care among children using a public hospital emergency department. Pediatric Emergency Care. 15(1):13-6, 1999 Feb.

OBJECTIVES: This study examined risk factors for not having a regular source of care among children presenting to an urban public hospital for nonappointment care. Lack of a regular source of care is associated with decreased use of appropriate health care services and preventive care among children.

METHODS: A cross-sectional survey was conducted for all children less than 16 years of age attending an emergency department at an urban public hospital over a consecutive 7-day period. Univariate and multivariate logistic regression analyses were conducted.

RESULTS: In 791 interviews available for analysis, 52% of preschool children and 66% of school-aged children did not have a regular source of care. Children without a regular source of care were more likely to present for nonurgent conditions (P < 0.0005). In **MULTIVARIATE** analysis, older age of the child (OR = 1.6, 95% CI 1.132.25), lack of insurance (OR = 1.47, 95% CI 1.03-2.11), and lack of personal vehicle (OR = 1.44, 95% CI 1.05-1.97) were associated with not having a regular source of care.

CONCLUSIONS: The majority of children using an urban emergency department were without a regular source of care. In this population, no single factor identified children without a regular source of care, but increased age and lack of insurance were associated with it. Addressing this situation will require a multifaceted approach that includes, but is not limited to, decreasing financial barriers.

Hypertension in the haemodialysis population: any relationship to 2-years survival? [see comments]. Nephrology, Dialysis, Transplantation. 14(1):125-8, 1999 Jan.

BACKGROUND: Few studies have quantified the effect of hypertension on survival in the haemodialysis (HD) population. We have previously reported lack of adverse effect of hypertension on 1-year mortality in a cohort of 649 haemodialysis patients (Am J Kidney Dis 1996; 28: 737-744). We report here the effect of hypertension on 2-year survival in the same cohort of patients.

METHODS: We reviewed the complete computerized files on 649 HD patients enrolled in 10 haemodialysis centres in the state of Mississippi, USA. One-month dialysis records for each patient from mid-October 1994 to mid-November 1994 were reviewed. Predialysis mean arterial pressure was calculated as immediate predialysis diastolic pressure plus one-third the difference between systolic and diastolic pressure. Patients were classified as hypertensive if their average pre-MAP was more than 114 mmHg or they were receiving antihypertensive drugs during the study period. Normotensives had a pre-MAP < 114 and were not receiving any antihypertensives. We followed these patients for 2 years to determine their survival and the effect of their BP status, as determined in October 1994, on 2-year mortality.

RESULTS: In univariate analysis, hypertension was associated with improved 2-years survival (relative risk 0.64, P=0.08 compared to normotensives). Furthermore, among the hypertensives, good blood pressure control (less than 140/90) was associated with increased relative risk of death at 2 years (RR 1.86, P=0.004). In **MULTIVARIATE** analysis, taking age, race, serum albumin, and diabetic status into consideration, there was a 27% reduction in mortality among hypertensives compared to normtensives (RR 0.73, P=0.06). Other factors of significance in multivariate analysis were age (RR 1.03/year, P=0.02), serum albumin (RR 0.36/g, P<0.0001), diabetes mellitus (RR 1.35, P=0.07), and race (RR 0.64, P=0.05).

CONCLUSIONS: Our study suggests that hypertension has no adverse effect on survival at 2 years in the haemodialysis population.

[Psychosocial risk factors in vulvovaginal mycosis. A multivariate long-term study]. [German]

Mycoses. 41 Suppl 2:49-53, 1998.

The results of a **MULTIVARIATE** logit-analysis of n = 9098 (female) patients of a gynecologic practice (from 1991 to 1994) confirm the relevance of psycho-social factors like employment, being married, smoking etc. on the incidence of the vulvovaginal mycosis. By the statistical results the studied factors can be rank-ordered from "smoking" as the most relevant to "virginity" as the most irrelevant factor. Surprisingly sexual contact and using oral contraception had no relevance. A check-list using factor-combinations enables to discriminate 48 types of female with different risk of incidence. The results of the study are in accordance with the following hypothesis: In most cases stress, induced by the psycho-social situation of the female and weakening the immune system, is the only responsible factor for the incidence of vulvovaginal mycosis.

Risk factors for human T cell lymphotropic virus type I among injecting drug users in northeast Brazil: possibly greater efficiency of male to female transmission.

Memorias do Instituto Oswaldo Cruz. 94(1):13-8, 1999 Jan-Feb.

It was observed in the city of Salvador, State of Bahia, the highest seroprevalence of human T cell lymphotropic virus type 1 (HTLV-I) infection in Brazil as demonstrated by national wide blood bank surveys. In this paper, we report results of an investigation of drug use and sexual behavior associated with HTLV-I infection among male and female injecting drug users (IDUs) in Salvador. A cross sectional study was conducted in the Historical District of Salvador from 1994-1996 (Projeto Brasil-Salvador) and 216 asymptomatic IDUs were selected using the snowball contact technique. Blood samples were collected for serological assays. Sera were screened for human immunodeficiency virus (HIV-1/2) and HTLV-I/II antibodies by ELISA and confirmed by Western blot. The overall prevalence of HTLV-I/II was 35.2% (76/216). The seroprevalence of HTLV-I, HTLV-II and HIV-I was for males 22%, 11.3% and 44.1% and for females 46.2%, 10.3% and 74.4% respectively. HTLV-I was identified in 72.4% of HTLV positive IDUs. Variables which were significantly associated with HTLV-I infection among males included needle sharing practices, duration of injecting drug use, HIV-I seropositivity and syphilis. Among women, duration of injecting drug use and syphilis were strongly associated with HTLV-I infection. **MULTIVARIATE** analysis did not change the direction of these associations. Sexual intercourse might play a more important role in HTLV-I infection among women than in men.

Influence of delay on survival in patients with breast cancer: a systematic review [see comments]. [Review] [103 refs]

Lancet. 353(9159):1119-26, 1999 Apr 3.

BACKGROUND: Most patients with breast cancer are detected after symptoms occur rather than through screening. The impact on survival of delays between the onset of symptoms and the start of treatment is controversial and cannot be studied in randomised controlled trials. We did a systematic review of observational studies (worldwide) of duration of symptoms and survival.

METHODS: We identified 87 studies (101,954 patients) with direct data linking delay (including delay by patients) and survival. We classified studies for analysis by type of data in the original reports: category I studies had actual 5-year survival data (38 studies, 53,912 patients); category II used actuarial or **MULTIVARIATE** analyses (21 studies, 25,102 patients); and category III was all other types of data (28 studies, 22,940 patients). We tested the main hypothesis that longer delays would be associated with lower survival, and a secondary hypothesis that longer delays were associated with more advanced stage, which would account for lower survival.

FINDINGS: In category I studies, patients with delays of 3 months or more had 12% lower 5-year survival than those with shorter delays (odds ratio for death 1.47 [95% CI 1.42-1.53]) and those with delays of 3-6 months had 7% lower survival than those with shorter delays (1.24 [1.17-1.30]). In category II, 13 of 14 studies with unrestricted samples showed a significant adverse relation between longer delays and survival, whereas four of five studies of only patients with operable disease showed no significant relation. In category III, all three studies with unrestricted samples supported the primary hypothesis. The 13 informative studies showed that longer delays were associated with more advanced stage. In studies that controlled for stage, longer delay was not associated with shorter survival when the effect of stage on survival was taken into account.

INTERPRETATION: Delays of 3-6 months are associated with lower survival. These effects cannot be accounted for by lead-time bias. Efforts should be made to keep delays by patients and providers to a minimum. [References: 103]

Prognostic impact of cyclin-dependent kinase inhibitor p27kip1 in node-positive breast cancer.

Journal of Surgical Oncology. 70(4):230-4, 1999 Apr.

BACKGROUND AND OBJECTIVES: p27kip1 (p27) plays an important role as a negative regulator of cell cycle-dependent kinase activity during progression of the cell cycle. The most important prognosticator of breast cancer is nodal status, and the aim of this study was to determine the prognostic implication of p27 in breast cancer patients with lymph node metastases.

METHODS: Immunohistochemical staining for p27 was performed on tissues from 102 patients with node-positive breast cancer.

RESULTS: A nuclear staining over 50% was defined as high expression. High expression of p27 was shown in 59 patients (57.8%). A significant correlation was found between high p27 and positive estrogen receptor status, but there was no correlation between p27 staining and age, menopausal status, nodal status, or tumor size. Low expression of p27 was significantly associated with shorter survival. A **MULTIVARIATE** analysis also showed that the only independent variable was p27.

CONCLUSIONS: The results indicated that low expression of p27 was an independent factor associated with poor prognosis. Therefore, p27 can be an important tool in making therapeutic decisions.

Tobacco smoking as a risk factor in anal carcinoma: an antiestrogenic mechanism?.

Journal of the National Cancer Institute. 91(8):708-15, 1999 Apr 21.

BACKGROUND: Human papillomavirus-associated anogenital carcinogenesis depends on poorly defined cofactors. Smoking was recently suggested to increase the risk of anal cancer more in premenopausal women than in postmenopausal women. Thus, we used our population-based anal cancer case-control study in Denmark and Sweden to test this hypothesis. METHODS: Our study included 417 patients (324 women and 93 men) who were diagnosed with anal cancer (84% invasive cancer) from 1991 through 1994; it also included five patients diagnosed in 1995. Two control groups were used: 1) 554 population control subjects (349 women and 205 men) and 2) 534 patients with rectal adenocarcinoma (343 women and 191 men). Odds ratios (ORs), calculated from logistic regression analyses, were used as measures of relative risk. All P values are two-sided.
RESULTS: Compared with the risk for lifelong nonsmokers, the risk of anal cancer was high among premenopausal women who currently smoked tobacco (**MULTIVARIATE** OR = 5.6; 95% confidence interval [CI] = 2.4-12.7) and increased linearly by .7% per pack-year smoked (one pack-year is equivalent to one pack of cigarettes smoked per day for 1 year) (P for trend <.001). Smoking was not statistically significantly associated with anal cancer risk in postmenopausal women or men. Women whose menstrual periods started late were at high risk (**MULTIVARIATE** OR = 3.6; 95% CI = 1.8-7.3, for >= 17 years of age versus < or = 12 years of age; P for trend <.001), and body mass index (weight in kg/[height in m]2) was inversely associated with risk among women (P<.001).
CONCLUSIONS: Because the risk of anal cancer associated with smoking was restricted to premenopausal women and because higher risk was associated with late menarche and lean body composition, female sex hormones may be a factor in anal cancer development in women. Since the anal mucosa is an estrogen-sensitive area, we hypothesize an antiestrogenic mechanism of action for smoking in anal carcinogenesis.

Soluble adhesion molecules in CSF are increased in children with severe head injury.

Journal of Neurotrauma. 15(10):777-87, 1998 Oct.

Leukocyte-endothelial adhesion molecules, critical to the development of acute inflammation, are expressed in brain as part of the acute inflammatory response to traumatic brain injury (TBI). We measured the concentrations of the adhesion molecules P-selectin, ICAM-1, E-selectin, L-selectin, and VCAM-1 in ventricular cerebrospinal fluid (CSF) from children with severe TBI (Glasgow coma score < 8) and compared these findings with those from children with bacterial meningitis. P-selectin, an adhesion molecule associated with ischemia/reperfusion, was increased in children with TBI versus meningitis and control. Univariate and **MULTIVARIATE** regression analyses demonstrated associations between CSF P-selectin and child abuse and age of < 4 years, and a significant, independent association between CSF intercellular adhesion molecule-1 (ICAM-1) and child abuse. These results are consistent with a specific acute inflammatory component to TBI in children. Future studies of secondary injury mechanisms and therapy after TBI should assess on the roles of P-selectin and ICAM-1 in injury and repair processes in brain after TBI.

Leg symptoms, the ankle-brachial index, and walking ability in patients with peripheral arterial disease.

Journal of General Internal Medicine. 14(3):173-81, 1999 Mar.

OBJECTIVE: To determine how functional status and walking ability are related to both severity of lower extremity peripheral arterial disease (PAD) and PAD-related leg symptoms.
DESIGN: Cross-sectional study. **SETTING**: Academic medical center.
PARTICIPANTS: Patients aged 55 years and older diagnosed with PAD in a blood flow laboratory or general medicine practice (n = 147). Randomly selected control patients without PAD were identified in a general medicine practice (n = 67).
MEASUREMENTS: Severity of PAD was measured with the ankle-brachial index (ABI). All patients were categorized according to whether they had (1) no exertional leg symptoms; (2) classic intermittent claudication; (3) exertional leg symptoms that also begin at rest (pain at rest), or (4) exertional leg symptoms other than intermittent claudication or pain at rest (atypical exertional leg symptoms). Participants completed the 36-Item Short-Form Health Survey (SF-36) and the Walking Impairment Questionnaire (WIQ). The WIQ quantifies patient-reported walking speed, walking distance, and stair-climbing ability, respectively, on a scale of 0 to 100 (100 = best).
MAIN RESULTS: In **MULTIVARIATE** analyses patients with atypical exertional leg symptoms, intermittent claudication, and pain at rest, respectively, had progressively poorer scores for walking distance, walking speed, and stair climbing. The ABI was measurably and independently associated with walking distance (regression coefficient = 2.87/0.1 ABI unit, p =.002) and walking speed (regression coefficient = 2.09/0.1 ABI unit, p =.015) scores. Among PAD patients only, pain at rest was associated independently with all WIQ scores and six SF-36 domains, while ABI was an independent predictor of WIQ distance score. CONCLUSIONS: Both PAD-related leg symptoms and ABI predict patient-perceived walking ability in PAD.

Impact of new guidelines on physicians' ordering of preoperative tests.

Journal of General Internal Medicine. 14(3):166-72, 1999 Mar.

OBJECTIVE: To compare the number of preoperative tests ordered for elective ambulatory surgery patients during the 2 years before and the 2 years after the establishment of new hospital testing guidelines.

MEASUREMENTS: The patterns of preoperative testing by surgeons and a medical consultant during the 2 years before and the 2 years after the establishment of new guidelines at one orthopedic hospital were reviewed. All tests ordered preoperatively were determined by review of medical records. Preoperative medical histories, physical examinations, and comorbidities were obtained according to a protocol by the medical consultant (author). Perioperative complications were determined by review of intraoperative and postoperative events, which also were recorded according to a protocol.

MAIN RESULTS: A total of 640 patients were enrolled, 361 before and 279 after the new guidelines. The mean number of tests decreased from 8.0 before to 5.6 after the new guidelines (p =.0001) and the percentage decrease for individual tests varied from 23% to 44%. Except for patients with more comorbidity and patients receiving general anesthesia, there were decreases across all patient groups. In **MULTIVARIATE** analyses only time of surgery (before or after new guidelines), age, and type of surgery remained statistically significant (p =.0001 for all comparisons). Despite decreases in surgeons' ordering of tests, the medical consultant did not order more tests after the new guidelines (p =.60) The majority of patients had no untoward events intraoperatively and postoperatively throughout the study period, with only 6% overall requiring admission to the hospital after surgery, mainly for reasons not related to abnormal tests. Savings from charges totaled $34,000 for the patients in the study.

CONCLUSIONS: Although there was variable compliance among physicians, new hospital guidelines were effective in reducing preoperative testing and did not result in increases in untoward perioperative events or in test ordering by the medical consultant.