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# Selected published abstracts of Baylor researchers

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## AMERICAN JOURNAL OF SURGERY

### Intermediate follow-up of carotid artery stent placement

Gable DR, Bergamini T, Garrett WV, Hise J, Smith BL, Shutze WP, Pearl G, Grimsley BR

(*Am J Surg* 2003;185:183–187) Copyright 2003. Reprinted with permission from Excerpta Medica Inc.

**Background:** Carotid artery stent placement (CAS) is becoming more popular among various specialties for the treatment of primary and recurrent carotid artery disease. The morbidity associated with this procedure is improving, but the intermediate- and long-term follow-up remains unknown. We report our restenosis rates and follow-up associated with CAS.

**Methods:** Thirty-one interventions on 29 patients from May 1998 to January 2002 were reviewed. All patients have undergone serial follow-up using Doppler ultrasound at 3 and 6 months and every 6 months thereafter. Ten interventions (32%) were performed on patients with recurrent carotid artery disease and 21 (68%) on patients with primary disease.

**Results:** Five periprocedural complications occurred (transient ischemic attack,  $n = 3$ ; major stroke,  $n = 1$ ; immediate intrastent restenosis requiring lysis,  $n = 1$ ) for a total immediate complication rate of 16%. No deaths occurred. Follow-up was achieved in all 29 patients (mean 28 months; range 20 to 46). Twenty-seven patients (29 vessels; 94%) remain asymptomatic with  $<50\%$  stenosis. Two vessels (6%) have been found to have a critical restenosis of  $>90\%$ . Both patients were symptomatic from their recurrence (transient ischemic attack,  $n = 1$ ; acute stroke,  $n = 1$ ). Cumulative major stroke and death rate including all follow-up was 6%.

**Conclusions:** CAS can be performed with an acceptable stroke/death rate (3%) in a properly selected patient population. In our small series of patients, the restenosis rate at a mean of 28 months after CAS is 6%.

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## ANNALS OF INTERNAL MEDICINE

### Cardiac events in patients undergoing noncardiac surgery: shifting the paradigm from noninvasive risk stratification to therapy

Grayburn PA, Hillis LD

(*Ann Intern Med* 2003;138:506–511)

Internists and cardiologists are often asked to estimate the risk for perioperative myocardial infarction or cardiac death in patients being considered for noncardiac surgery. Estimating this risk in an individual patient is difficult and complex. Although noninvasive imaging tests are often used for this purpose, a review of the literature reveals that the positive predictive value of noninvasive imaging tests is uniformly low and that they do not provide information beyond that obtained by assessing simple clinical risk variables. Moreover, no evidence exists that noninvasive imaging tests lead to a therapeutic strategy that reduces the risk for perioperative myocardial infarction or cardiac death. Since the publication of guidelines for preoperative risk stratification by the American College of Cardiology/American Heart Association in 1996 and the American College of Physicians in 1997, 3 clinical trials have shown that beta-blocker therapy reduces the risk for perioperative cardiac events. This paper focuses on the relationship between risk stratification and subsequent therapy to minimize or eliminate risk. In short, the paradigm is shifting from predicting which patient is at high risk for having a perioperative cardiac event to minimizing the likelihood of such an event with specific perioperative pharmacologic therapy.

BUMC PROCEEDINGS 2003;16:373–376

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## ANNALS OF SURGICAL ONCOLOGY

### Preliminary outcome analysis in patients with breast cancer and a positive sentinel lymph node who declined axillary dissection

Fant JS, Grant MD, Knox SM, Livingston SA, Ridl K, Jones RC, Kuhn JA

(*Ann Surg Oncol* 2003;10:126–130)

**Background:** This retrospective study was designed to provide a preliminary outcome analysis in patients with positive sentinel nodes who declined axillary dissection.

**Methods:** A review was conducted of patients who underwent lumpectomy and sentinel lymph node excision for invasive disease between January 1998 and July 2000. Those who were found to have sentinel lymph node metastasis without completion axillary dissection were selected for evaluation. Follow-up included physical examination and mammography.

**Results:** Thirty-one patients were identified who met inclusion criteria. Primary invasive cell types included infiltrating ductal carcinoma, infiltrating lobular carcinoma, and mixed cellularity. Most primary tumors were T1. Nodal metastases were identified by hematoxylin and eosin stain and immunohistochemistry. Twenty-seven of the metastases were microscopic ( $<2$  mm), and the remaining 4 were macroscopic. All patients received adjuvant systemic therapy. With a mean follow-up of 30 months, there have been no patients with axillary recurrence on physical examination or mammographic evaluation.

**Conclusions:** We have presented patients with sentinel lymph nodes involved by cancer who did not undergo further axillary resection and remain free of disease at least 1 year later. This preliminary analysis supports the inclusion of patients with subclinical axillary disease in trials that randomize to observation alone.

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## DIABETES CARE

### Pramlintide as an adjunct to insulin therapy improves long-term glycemic and weight control in patients with type 2 diabetes: a 1-year randomized controlled trial

Hollander PA, Levy P, Fineman MS, Maggs DG, Shen LZ, Strobel SA, Weyer C, Kolterman OG

(*Diabetes Care* 2003;26:784–790)

**Objective:** Mealtime amylin replacement with the human amylin analog pramlintide, as an adjunct to mealtime insulin replacement, reduces postprandial glucose excursions in patients with type 2 diabetes. The aim of the present study was to assess the long-term efficacy and safety of pramlintide in this patient population.

**Research design and methods:** In a 52-week, double-blind, placebo-controlled, parallel-group, multicenter study, 656 patients with type 2 diabetes (age  $57 \pm 10$  years, diabetes duration  $12 \pm 7$  years, BMI  $34.0 \pm 7.0$  kg/m<sup>2</sup>, HbA<sub>1c</sub>  $9.1 \pm 1.2\%$ , mean  $\pm$  SD) treated with insulin (alone or in combination with sulfonylureas and/or metformin) were randomized to receive additional preprandial subcutaneous injections of either placebo or pramlintide (60  $\mu$ g TID, 90  $\mu$ g BID, or 120  $\mu$ g BID).

**Results:** Treatment with pramlintide 120  $\mu$ g BID led to a sustained reduction from baseline in HbA<sub>1c</sub> ( $-0.68$  and  $-0.62\%$  at weeks 26 and 52, respectively), which was significantly greater than that seen with placebo ( $P < 0.05$ ). The proportion of patients achieving an HbA<sub>1c</sub>  $<8\%$  was approximately twofold greater with pramlintide (120  $\mu$ g BID) than with placebo

(46 vs 28%,  $P < 0.05$ ). The glycemic improvement with pramlintide 120  $\mu\text{g}$  BID was accompanied by a mean weight loss ( $-1.4$  kg vs  $+0.7$  kg with placebo at week 52,  $P < 0.05$ ) and occurred without an overall increase in the severe hypoglycemia event rate. The most common adverse event associated with pramlintide use was transient, mild-to-moderate nausea.

**Conclusions:** Mealtime amylin replacement with pramlintide 120  $\mu\text{g}$  BID, as an adjunct to insulin therapy, improves long-term glycemic and weight control in patients with type 2 diabetes.

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## EXPERT OPINION ON BIOLOGICAL THERAPY

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### Modulating T cell responses for the treatment of psoriasis: a focus on efalizumab

Cather JC, Cather JC, Menter A

(*Expert Opin Biol Ther* 2003;3:361–370)

An improved understanding regarding the pathophysiology of psoriasis, coupled with advances in molecular research, has prompted the development of targeted biologic treatments for patients with plaque psoriasis. T lymphocytes play an important role in initiating the immune system and the inflammatory responses that result in the development and maintenance of psoriatic plaques. Efalizumab (anti-CD11a, Raptiva; Genentech, Inc) is a mAb that targets the T-cell adhesion molecule, leukocyte function-associated antigen-1 (LFA-1). By binding to CD11a—the alpha-subunit of LFA-1—LFA-1 is prevented from binding with its ligand, intercellular adhesion molecule-1 (ICAM-1). This inhibits various T-cell processes believed to be important in the pathogenesis of psoriasis, including T-cell activation, T-cell adhesion to endothelial cells, and T-cell migration. Clinical trials demonstrate that efalizumab, given subcutaneously once weekly, provides clinical benefit, including improved quality of life, in patients with moderate-to-severe plaque psoriasis. Efalizumab is associated with an early onset of action, with improvement noted as early as 14 days. Studies with extended treatment suggest that continuing efalizumab therapy is more beneficial in maintaining and improving responses. Relapse of psoriasis is usually seen within 60–70 days after discontinuation of therapy, and rebound in ~5% of patients (i.e., flare to  $>125\%$  of baseline) is noted. Efalizumab is associated with acute adverse events during the first and second injections, which decrease in incidence with each subsequent injection. Data indicate that efalizumab can be safely administered for extended periods of time. Given the efficacy, early onset of clinical benefit, the safety profile and the convenience of once-weekly subcutaneous home dosing, efalizumab offers an interesting new therapeutic option for the treatment of psoriasis and the potential for improved and potentially safer long-term, continuous “maintenance” therapy.

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## INTERNATIONAL JOURNAL OF DERMATOLOGY

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### Repeat courses of intravenous alefacept in patients with chronic plaque psoriasis provide consistent safety and efficacy

Lowe NJ, Gonzalez J, Bagel J, Caro I, Ellis CN, Menter A

(*Int J Dermatol* 2003;42:224–230)

**Background:** Psoriasis is a chronic, relapsing skin disease that may require multiple treatment courses. Alefacept targets the memory T cells implicated in psoriasis pathogenesis. This open-label study evaluated the safety and tolerability, efficacy, and pharmacodynamics of repeat courses of alefacept in men and women with chronic plaque psoriasis. This article reports the interim results of this ongoing study.

**Methods:** Patients ( $n = 174$ ) who participated in previous phase II studies of alefacept were included in this retreatment study. Intravenous alefacept (7.5 mg) was administered once weekly for 12 weeks followed by 12 weeks of observation. Initial and subsequent retreatment courses were only given when, in the opinion of the investigators, disease had returned and neces-

sitated treatment; CD4<sup>+</sup> T-cell counts had to be at or above the lower limit of normal.

**Results:** Adverse events were similar regardless of the retreatment course. No opportunistic infections, rebound of disease, or flares were reported. Low titers of anti-alefacept antibodies occurred in a few patients without related safety issues. Sixty-six percent of patients achieved a  $\geq 50\%$  reduction in the Psoriasis Area and Severity Index (PASI) at any time after the first dose of retreatment course 1. Patients who received 2 retreatment courses ( $n = 50$ ) had consistent or improved responses after the second course; 64% and 68% of these patients achieved a  $\geq 50\%$  PASI improvement at any time after the first dose of retreatment courses 1 and 2, respectively. Alefacept selectively reduced memory T cells without cumulative effects.

**Conclusions:** Repeat courses of alefacept were well tolerated, and subsequent retreatment courses were at least as effective as the initial course of therapy.

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## JOURNAL OF EXPERIMENTAL MEDICINE

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### Interferon and granulopoiesis signatures in systemic lupus erythematosus blood

Bennett L, Palucka AK, Arce E, Cantrell V, Borvak J, Banchereau J, Pascual V

(*J Exp Med* 2003;197:711–723) Reproduced by copyright permission of The Rockefeller University Press.

Systemic lupus erythematosus (SLE) is a prototype systemic autoimmune disease characterized by flares of high morbidity. Using oligonucleotide microarrays, we now show that active SLE can be distinguished by a remarkably homogeneous gene expression pattern with overexpression of granulopoiesis-related and interferon (IFN)-induced genes. Using the most stringent statistical analysis (Bonferroni correction), 15 genes were found highly up-regulated in SLE patients, 14 of which are targets of IFN and one, defensin DEFA-3, a major product of immature granulocytes. A more liberal correction (Benjamini and Hochberg correction) yielded 18 additional genes, 12 of which are IFN-regulated and 4 granulocyte-specific. Indeed, immature neutrophils were identified in a large fraction of SLE patients' white blood cells. High-dose glucocorticoids, a standard treatment of disease flares, shuts down the interferon signature, further supporting the role of this cytokine in SLE. The expression of 10 genes correlated with disease activity according to the SLEDAI. The most striking correlation ( $P < 0.001$ ,  $r = 0.55$ ) was found with the formyl peptide receptor-like 1 protein that mediates chemotactic activities of defensins. Therefore, while the IFN signature confirms the central role of this cytokine in SLE, microarray analysis of blood cells reveals that immature granulocytes may be involved in SLE pathogenesis.

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## JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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### Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD trial

Young YB, Abraham WT, Smith AL, Leon AR, Lieberman R, Wilkoff B, Canby RC, Schroeder JS, Liem LB, Hall S, Wheelan K, for the Multi-center InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) trial investigators

(*JAMA* 2003;289:2685–2694) Copyrighted 2003, American Medical Association.

**Context:** Cardiac resynchronization therapy (CRT) through biventricular pacing is an effective treatment for heart failure (HF) with a wide QRS; however, the outcomes of patients requiring CRT and implantable cardioverter defibrillator (ICD) therapy are unknown.

**Objective:** To examine the efficacy and safety of combined CRT and ICD therapy in patients with New York Heart Association (NYHA) class III or IV congestive HF despite appropriate medical management.

**Design, setting, and participants:** Randomized, double-blind, parallel-controlled trial conducted from October 1, 1999, to August 31, 2001, of 369 patients with left ventricular ejection fraction of 35% or less, QRS duration of 130 ms, at high risk of life-threatening ventricular arrhythmias, and in NYHA class III (n = 328) or IV (n = 41) despite optimized medical treatment.

**Interventions:** Of 369 randomized patients who received devices with combined CRT and ICD capabilities, 182 were controls (ICD activated, CRT off) and 187 were in the CRT group (ICD activated, CRT on).

**Main outcome measures:** The primary double-blind study end points were changes between baseline and 6 months in quality of life, functional class, and distance covered during a 6-minute walk. Additional outcome measures included changes in exercise capacity, plasma neurohormones, left ventricular function, and overall HF status. Survival, incidence of ventricular arrhythmias, and rates of hospitalization were also compared.

**Results:** At 6 months, patients assigned to CRT had a greater improvement in median (95% confidence interval) quality of life score (-17.5 [-21 to -14] vs -11.0 [-16 to -7],  $P = .02$ ) and functional class (-1 [-1 to 0] vs 0 [-1 to 0],  $P = .007$ ) than controls but were no different in the change in distance walked in 6 minutes (55 m [44-79] vs 53 m [43-75],  $P = .36$ ). Peak oxygen consumption increased by 1.1 mL/kg per minute (0.7-1.6) in the CRT group vs 0.1 mL/kg per minute (-0.1 to 0.8) in controls ( $P = .04$ ), although treadmill exercise duration increased by 56 seconds (30-79) in the CRT group and decreased by 11 seconds (-55 to 12) in controls ( $P < .001$ ). No significant differences were observed in changes in left ventricular size or function, overall HF status, survival, and rates of hospitalization. No proarrhythmia was observed and arrhythmia termination capabilities were not impaired.

**Conclusions:** Cardiac resynchronization improved quality of life, functional status, and exercise capacity in patients with moderate to severe HF, a wide QRS interval, and life-threatening arrhythmias. These improvements occurred in the context of underlying appropriate medical management without proarrhythmia or compromised ICD function.

### Changes in rates of autopsy-detected diagnostic errors over time: a systematic review

Shojania KG, Burton EC, McDonald KM, Goldman L

(JAMA 2003;289:2849-2856) Copyrighted 2003, American Medical Association.

**Context:** Substantial discrepancies exist between clinical diagnoses and findings at autopsy. Autopsy may be used as a tool for quality management to analyze diagnostic discrepancies.

**Objective:** To determine the rate at which autopsies detect important, clinically missed diagnoses and the extent to which this rate has changed over time.

**Data sources:** A systematic literature search for English-language articles available on MEDLINE from 1966 to April 2002, using the search terms *autopsy*, *postmortem changes*, *post-mortem*, *postmortem*, *necropsy*, and *post-humous*, identified 45 studies reporting 53 distinct autopsy series meeting prospectively defined criteria. Reference lists were reviewed to identify additional studies, and the final bibliography was distributed to experts in the field to identify missing or unpublished studies.

**Study selection:** Included studies reported clinically missed diagnoses involving a primary cause of death (major errors), with the most serious being those likely to have affected patient outcome (class I errors).

**Data extraction:** Logistic regression was performed using data from 53 distinct autopsy series over a 40-year period and adjusting for the effects of changes in autopsy rates, country, case mix (general autopsies; adult medical; adult intensive care; adult or pediatric surgery; general pediatrics or pediatric inpatients; neonatal or pediatric intensive care; and other autopsy), and important methodological features of the primary studies.

**Data synthesis:** Of 53 autopsy series identified, 42 reported major errors and 37 reported class I errors. Twenty-six autopsy series reported both major and class I error rates. The median error rate was 23.5% (range, 4.1%-49.8%) for major errors and 9.0% (range, 0%-20.7%) for class I errors. Analyses of diagnostic error rates adjusting for the effects of case mix, country, and autopsy rate yielded relative decreases per decade of 19.4% (95% confidence interval [CI], 1.8%-33.8%) for major errors and 33.4% (95% [CI], 8.4%-51.6%) for class I errors. Despite these decreases, we estimated that a contemporary US institution (based on autopsy rates ranging from 100% [the extrapolated extreme at which clinical selection is eliminated] to 5% [roughly the national average]) could observe a major error rate from 8.4% to 24.4% and a class I error rate from 4.1% to 6.7%.

**Conclusion:** The possibility that a given autopsy will reveal important unsuspected diagnoses has decreased over time but remains sufficiently high that encouraging ongoing use of the autopsy appears warranted.

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## LIVER TRANSPLANTATION

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### Projecting future complications of chronic hepatitis C in the United States

Davis GL, Albright JE, Cook SF, Rosenberg DM

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Chronic hepatitis C virus (HCV) infection is common and often results in slowly progressive liver disease. Although acute hepatitis C is now uncommon, most patients with acute infection have developed chronic hepatitis, and, therefore, the pool of infected patients is large. We used a modification of a previously described natural history model for HCV infection to project the number of cases of HCV infection, cirrhosis, and liver failure over the next 40 years. The model estimated the prevalence of HCV infection in the United States was  $3.07 \times 10^6$  in 1993 (compared with an adjusted National Health and Nutrition Evaluation Survey [NHANES] III estimate of 2.8 to  $3.5 \times 10^6$ ). A gradual decline in the prevalence of infection should occur by year 2040 because of aging and natural deaths among the infected pool. However, as the duration of infection increases in the surviving cohort, the proportion with cirrhosis will increase from 16% to 32% by 2020 in an untreated population. Complications of cirrhosis also will increase dramatically over the next 20 years: hepatic decompensation (up 106%), hepatocellular carcinoma (up 81%), and liver-related deaths (up 180%). Although current treatment regimens eradicate HCV in over 50% of cases, many more patients would need to be treated to significantly impact disease progression. Identification and treatment of every case of HCV infection (with or without cirrhosis) would reduce the number of cases of decompensated cirrhosis by almost half after 20 years. Despite the declining incidence of acute HCV infection, chronic hepatitis C is common. The prevalence of cirrhosis and the incidence of its complications will increase over the next 10 to 20 years, because the duration of infection increases among those with chronic hepatitis C. These data emphasize the need for greater access to transplantation by expansion of the donor pool, increasing use of split livers and living donors, and novel options such as xenotransplantation.

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## PEDIATRIC TRANSPLANTATION

### Liver transplantation for cholestasis associated with cystic fibrosis in the pediatric population

Molmenti EP, Squires RH, Nagata D, Roden JS, Molmenti H, Fasola CG, Prestidge C, D'Amico L, Casey D, Sanchez EQ, Goldstein RM, Levy MF, Benser M, McPhail W, Andrews W, Andersen JA, Klintmalm GB

(*Pediatr Transplant* 2003;7:93–97)

The most common hepatic complications of cystic fibrosis (CF) are steatosis, fibrosis, biliary cirrhosis, atretic gallbladder, cholelithiasis, and sclerosing cholangitis. Cholestatic liver disease is a slow progressive disorder but will stabilize for many patients. CF patients may suffer from the consequences of their liver disease and without liver transplantation, variceal hemorrhage, malnutrition, or end-stage liver disease can lead to death. Prospective data were collected and reviewed on 311 liver transplants performed in 283 patients at the Children's Medical Center of Dallas between October 1984 and November 2000. Ten children received an orthotopic liver transplant (OTLX) for end-stage liver disease associated with cystic fibrosis. Pulmonary function tests were obtained preoperatively in all cases. There were 9 boys and 1 girl. Six are currently alive, and 4 are dead. Both patient and graft survival was 5.75 yr. Among those currently alive, mean patient and graft survival is 7.71 yr (range 0.10–12.62 yr). Mean patient and graft survival of those who died was 2.35 yr (range 0.78–5.33 yr). No survivor required retransplantation and, currently, all have normal serum aminotransferase values. Chronic sinusitis was not a significant pre- or posttransplant morbidity, although systematic radiographic evaluation of the sinuses did not occur. Pulmonary deaths occurred in 3 patients from pulmonary hemorrhage, pulmonary infection with *Aspergillus* and *Candida glabrata*, and acute bronchopneumonia associated with polymicrobial sepsis because of *Pseudomonas*, *Klebsiella*, and *Candida albicans* 1.44, 0.78, and 1.83 yr, respectively, after transplantation. The fourth death was associated with chronic rejection and occurred 5.33 yr after transplantation. All nonsurvivors were below the fifth percentile for height and weight at the time of liver transplantation. Mean age at transplantation was 9.72 yr (range 1.23–19.09, median 9.61). Survivors were transplanted at a younger age than nonsurvivors (mean of 9.21 yr vs 10.66 yr) and had shorter waiting times from diagnosis of end-stage liver disease to transplantation (6.87 months vs 13.83 months). Eighty percent (n = 8) of patients had pretransplant variceal bleeds (83% of survivors, 75% of nonsurvivors). While all nonsurvivors had a history of meconium ileus and preoperative need of pancreatic enzymes, only 67% of those alive experienced these complications. Preoperative forced vital capacity (FVC) was 103% for survivors and 95% for nonsurvivors. The corresponding numbers for forced expiratory flow (FEF) 25–75 were 74%–84%, respectively. Preoperative *Aspergillus* was identified in 30% of patients (n = 3). Two of these patients are alive. Cystic fibrosis constitutes an indication for 3.5% of pediatric liver transplants. Evaluation and transplantation for end-stage liver disease associated with cystic fibrosis should be undertaken at an early age. Most deaths were associated with pulmonary/septic events and occurred <2 yr after OLTX. Those children who did not survive had poor growth and nutrition, prolonged waiting times prior to transplantation, were transplanted at an older age, and had a higher incidence of pancreatic insufficiency and meconium ileus. The presence of *Aspergillus* in the sputum does not constitute a contraindication for OLTX.

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## PEDIATRICS

### Clinical effects of L-carnitine supplementation on apnea and growth in very low birth weight infants

Whitfield J, Smith T, Sollohub H, Sweetman L, Roe CR

(*Pediatrics* 2003;111:477–482)

**Objective:** Systemic carnitine deficiency may present with apnea, hypotonia, and poor growth. Premature infants often manifest these symptoms and are at risk of developing carnitine deficiency because of immaturity of the biosynthetic pathway, lack of sufficient predelivery transplacental transport, and lack of sufficient exogenous supplementation. This study was undertaken to examine the effect of carnitine supplementation in premature infants.

**Methods:** Eighty preterm infants <1500 g were enrolled in a prospective, double-blind, placebo-controlled study of carnitine supplementation within 96 hours of delivery. Growth, length of hospital stay, and frequency and severity of apnea were the primary outcome measures.

**Results:** Weight gain and change in length, fronto-occipital head circumference, mid arm circumference, and triceps skinfold thickness were similar between the carnitine-supplemented and placebo groups. The amount and severity of apnea and the overall length of hospitalization were also similar between the 2 groups. The carnitine levels in the supplemented group were significantly higher than in the placebo group at 4 and 8 weeks after study entry.

**Conclusion:** Although preterm infants <1500 g have low carnitine levels, routine supplementation with carnitine has no demonstrable effect on growth, apnea, or length of hospitalization and thus seems to be unnecessary.

### Evaluation and development of potentially better practices to prevent neonatal nosocomial bacteremia

Kilbride HW, Powers R, Wirtschafter DD, Sheehan MB, Charsha DS, LaCorte M, Finer N, Goldmann DA

(*Pediatrics* 2003;111(4 Part 2):E504–E518)

**Objective:** Six neonatal intensive care units (NICUs) that are members of the Vermont Oxford National Evidence-Based Quality Improvement Collaborative for Neonatology collaborated to reduce infection rates. There were 7 centers in the original focus group, but 1 center left the collaborative after 1 year. The objective of this study was to develop strategies to decrease nosocomial infection rates in NICUs.

**Methods:** The process included a comprehensive literature review, internal practice analyses, benchmark studies, and development of practical experience through rapid-cycle changes, subsequent analysis, and feedback. This process led to 3 summary statements on potentially better practices in handwashing, approach to nosocomial sepsis evaluations, and central venous catheter management.

**Results:** These statements provide a basis for an evidence-based approach to lowering neonatal intensive care unit nosocomial infection rates.

**Conclusions:** The 2-year process also led to changes in the culture and habits of the institutions involved, which should in turn have long-term effects on other aspects of quality improvement.