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## Selected published abstracts of Baylor researchers

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### AMERICAN JOURNAL OF CARDIOLOGY

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#### Do prehospital discharge pacemaker checks provide any additional clinical benefit?

Wheelan KR, Legge DM, Sakowski BC, Bruce SS, Roberts DC, Johnston LM, Moore BJ, Beveridge TP, Wells PJ, Vallabahn R, Donsky MS, Franklin JO

*Am J Cardiol* 2005;96(3):414–416. Copyright 2005. Reprinted with permission from Excerpta Medica, Inc.

We performed a retrospective analysis of 250 records of consecutive, newly implanted, pacemaker patients from a single center to determine the rate of postimplant complications and observations discovered before and during the prehospital discharge evaluation. No observations occurred in 246 of 250 patients (98.4%) (1-sided 95% confidence interval 96.4%). Of the 250 patients, 4 had observations that were discovered at the prehospital discharge check and required reprogramming to increase the sensitivity safety margin (3 atrial and 1 ventricular). We documented only 1 complication that was discovered before the predischarge evaluation through telemetry and resulted in an atrial lead revision.

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### CLINICAL BREAST CANCER

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#### Phase II study of pemetrexed in patients pretreated with an anthracycline, a taxane, and capecitabine for advanced breast cancer

O'Shaughnessy JA, Clark RS, Blum JL, Mennel RG, Snyder D, Ye Z, Liepa AM, Melemed AS, Yardley DA

*Clin Breast Cancer* 2005;6(2):143–149. Reprinted with permission from Cancer Information Group.

**Background:** This phase II study evaluated the efficacy, safety, and health outcomes of pemetrexed treatment in heavily pretreated patients with advanced breast cancer.

**Patients and methods:** Women with metastatic breast cancer, Karnofsky performance status  $\geq 70$ , and previous treatment with  $\geq 3$  regimens containing anthracyclines, taxanes, and capecitabine were eligible. Pemetrexed 500 mg/m<sup>2</sup> intravenous infusion was administered on day 1 of a 21-day treatment cycle.

**Results:** Eighty patients were enrolled, and 60 received concurrent folic acid and vitamin B<sub>12</sub> supplements per protocol amendment to minimize possible pemetrexed-related toxicity. The median numbers of cycles delivered were 3 for vitamin-supplemented patients and 2 for non-vitamin-supplemented patients. Regardless of vitamin supplementation, the overall response rate was 8% (95% CI, 3%–16.6%), stable disease was exhibited in 36% of patients, median time to disease progression was 2.9 months, and median survival was 8.2 months. Improvements in patient-reported symptoms ranged from 16.2% for pain intensity to 32.1% for nausea. Major grade 3/4 toxicities were hematologic, with grade 4 neutropenia in 10% of patients and grade 3 toxicities consisting primarily of neutropenia (29%) and leukopenia

(21%). There were no clear trends of the effect of supplementation on toxicity.

**Conclusion:** Pemetrexed has modest antitumor activity and is well tolerated in heavily pretreated patients with breast cancer. Further evaluation of this multitargeted antifolate in advanced breast cancer is warranted.

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### GASTROENTEROLOGY

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#### Stimulated active potassium secretion in a patient with colonic pseudo-obstruction: a new mechanism of secretory diarrhea

van Dinter TG Jr, Fuerst FC, Richardson CT, Santa Ana CA, Polter DE, Fordtran JS, Binder HJ

*Gastroenterology* 2005;129(4):1268–1273. Reprinted with permission from the American Gastroenterological Association.

**Background and aims:** Secretory diarrhea is caused by inhibition of intestinal active sodium absorption and stimulation of active chloride secretion. The resulting increase in fecal sodium salts causes an isotonic increase in fecal water output. Abnormalities in potassium transport are not known to be a cause of secretory diarrhea. The aim of our report is to describe a patient with secretory diarrhea that was mediated by excess intestinal secretion of potassium.

**Methods:** A 78-year-old woman developed colonic pseudo-obstruction, complicated by severe diarrhea and hypokalemia. Her stools were collected quantitatively on 11 occasions and analyzed for electrolyte concentrations. Rectosigmoid potential difference was measured.

**Results:** The diarrheal fluid had a very high potassium concentration (130–170 mEq/L) and a very low sodium concentration (4–15 mEq/L). Stool potassium losses were as high as 256 mEq/day (normal, 9 mEq/day), and fecal sodium losses were never higher than 13 mEq/day. Potential difference between colonic lumen and a peripheral reference electrode was  $-14$  mV (lumen side negative).

**Conclusions:** Fecal potassium salts were the exclusive driving force for severe secretory diarrhea in a patient with colonic pseudo-obstruction. The high fecal output of potassium was due to stimulation of active colonic potassium secretion, possibly because of changes in autonomic nervous system activity and distention of the colon in association with colonic pseudo-obstruction. The extremely low fecal excretion of sodium indicates that active sodium absorption was not inhibited. This case study reveals an ion transport mechanism of secretory diarrhea that has not been previously appreciated.

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### LANCET INFECTIOUS DISEASES

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#### Treatment of chronic hepatitis C infection: one step at a time

Davis GL, Lindsay KL

*Lancet Infect Dis* 2005;5(8):524–526. Copyright 2005. Reprinted with permission from Elsevier.

Non-A, non-B hepatitis was recognized as an important cause of chronic liver disease long before the aetiological agent—hepatitis C virus—was identified in 1989. Recombinant interferons, initially developed as a

treatment for malignancies, proved to be an effective treatment for this disease before the identification of the viral agent. Subsequent testing for hepatitis C virus RNA demonstrated that the virus appeared to be eradicated in a small proportion of treated patients. Treatment regimens have improved dramatically since 1989 with the addition of the oral nucleoside ribavirin and long-acting pegylated interferons to treatment regimens. Currently, more than half of treated patients can achieve durable viral clearance. This clearance is quite a remarkable feat; indeed, eradication is not possible in any other chronic viral infection. Considerable effort continues to be devoted to improving therapeutic regimens to make them more effective and tolerable. Drugs that directly act on the replicative machinery of the virus—protease and polymerase inhibitors—are under development and entering clinical trials in human beings.

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## LIVER TRANSPLANTATION

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### **A randomized, open-label study to evaluate the safety and pharmacokinetics of human hepatitis C immune globulin (Civacir) in liver transplant recipients**

Davis GL, Nelson DR, Terrault N, Pruett TL, Schiano TD, Fletcher CV, Sapan CV, Riser LN, Li Y, Whitley RJ, Gnann JW Jr

*Liver Transpl* 2005;11(8):941–949. Copyright 2005, American Association for the Study of Liver Diseases. Reprinted with permission of Wiley-Liss Inc., a subsidiary of John Wiley & Sons Inc.

Chronic hepatitis C is the most common indication for liver transplantation, but viral recurrence is universal and progressive graft injury occurs in most recipients. Our aim was to assess the safety, pharmacokinetics (PK), and antiviral effects of high doses of a human hepatitis C antibody enriched immune globulin product (HCIG) in patients undergoing liver transplantation for chronic hepatitis C. This was a multicenter, randomized, open-label, controlled trial conducted at 4 transplant centers in the United States. A total of 18 patients with chronic hepatitis C, who underwent liver transplantation, were randomized to receive low-dose HCIG (75 mg/kg) or high-dose HCIG (200 mg/kg), or no treatment. A total of 17 infusions of HCIG were administered in each treated patient over 14 weeks using a time-dependent dosing strategy based on the PK of anti-hepatitis B immune globulin in liver transplant recipients. Hepatitis C virus levels, liver enzymes, and liver biopsies were obtained serially throughout the study period. PK profiles of HCV antibodies were determined on days 4, 10, and 98. HCIG infusions were safe and tolerated. The infusion rate could not be maximized because of symptoms for 18% to 30% of the doses. The half-life of HCIG was extremely short immediately after transplantation but was gradually prolonged. In the high-dose group, serum alanine aminotransferase (ALT) levels normalized in most subjects and no patient developed hepatic fibrosis. However, serum HCV RNA levels were not suppressed at either dose. In conclusion, HCIG, an anti-HCV enriched immune globulin product, appears to be safe in patients with chronic hepatitis C undergoing liver transplantation. Further studies are required to determine whether the drug has beneficial effects in this group of patients.

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## JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

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### **Cutaneous lymphoid hyperplasia and marginal zone B-cell lymphoma following vaccination**

May SA, Netto G, Domiati-Saad R, Kasper C

*J Am Acad Dermatol* 2005;53(3):512–516. Copyright 2005. Reprinted with permission from the American Academy of Dermatology.

Atypical lymphoid infiltrations arose within the influenza inoculation sites of two adult female patients. One patient developed a low-grade cutaneous marginal zone B-cell lymphoma (MZL) that was responsive to local excision and radiation therapy despite spread to a distant cutaneous site. The second patient's clinical course was characterized by a locally aggressive, histologically reactive inflammatory reaction responsive only to radiation therapy after multiple failed attempts at surgical resection.

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## JOURNAL OF IMMUNOTHERAPY

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### **Immune and clinical outcomes in patients with stage IV melanoma vaccinated with peptide-pulsed dendritic cells derived from CD34<sup>+</sup> progenitors and activated with type I interferon**

Banchereau J, Ueno H, Dhodapkar M, Connolly J, Finholt JP, Klechevsky E, Blanck JP, Johnston DA, Palucka AK, Fay J

*J Immunother* 2005;28(5):505–516. Reprinted with permission from Lippincott Williams & Wilkins.

Twenty-two HLA A\*0201<sup>+</sup> patients with stage IV melanoma were enrolled in a phase 1 safety and feasibility trial using a composite dendritic cell (DC) vaccine generated by culturing CD34<sup>+</sup> hematopoietic progenitors and activated with IFN- $\alpha$ . The DC vaccine was loaded with peptides derived from four melanoma tissue differentiation antigens (MART-1, tyrosinase, MAGE-3, and gp100) and influenza matrix peptide (Flu-MP). Twenty patients were evaluable, 14 of whom received vaccination with peptide-pulsed DCs without keyhole limpet hemocyanin (KLH) and 6 of whom received vaccination with KLH-loaded DCs. Patients were vaccinated until disease progression or until they had received eight vaccinations. None of the analyzed patients showed the expansion of melanoma-peptide-specific circulating effector memory T cells that secrete IFN- $\gamma$  in direct ELISPOT. Melanoma-peptide-specific recall memory CD8<sup>+</sup> T cells able to secrete IFN- $\gamma$  and to proliferate could be detected in six of the seven analyzed patients. There were no objective clinical responses. The estimated median overall survival was 12 months (range 2–38), and the median event-free survival was 4 months (range 1–12). There was no statistically significant survival advantage in patients who received KLH-loaded vaccines. As of March 2005, four patients remained alive, 26+, 28+, 28+, and 36+ months. Three of them had received KLH-loaded vaccines and all of them had had additional therapy. Overall, these results suggest that IFN- $\alpha$ -activated CD34-DCs are safe but elicit only limited immune responses, underscoring the need to test different DC maturation factors.

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## MOLECULAR INTERVENTIONS

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### Chemoprevention goes gourmet: different flavors of NO-aspirin

Goel A, Gasche C, Boland CR

*Mol Interv* 2005;5(4):207–210. Reprinted with permission from the American Society for Pharmacology and Experimental Therapeutics.

Among the salutary effects of aspirin (acetylsalicylic acid, ASA) are its ability to keep platelets from aggregating and blood from clotting too readily, to reduce fever, and to ameliorate inflammation. Aspirin also is beneficial in preventing colorectal cancer; however, aspirin is not without its side effects, which include gastrointestinal irritation and ulceration. Additionally, if a patient has pre-existing conditions that are exacerbated by aspirin, does a daily dose of aspirin make sense, when admittedly, the reduction of the incidence of colorectal cancer is less than 50% in those who take aspirin daily? New research on nitric oxide–modified aspirin (NO-ASA) indicates that the gastrointestinal side effects might be suppressed while keeping or enhancing the ability of the modified aspirin to prevent colorectal cancer and inhibit the proliferation of cancer cells in vitro.

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## MOLECULAR THERAPY

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### GM-CSF gene-transduced tumor vaccines

Eager R, Nemunaitis J

*Mol Ther* 2005;12(1):18–27. Copyright 2005. Reprinted with permission from Elsevier.

GVAX is a GM-CSF gene-transduced tumor vaccine. Expression of the GM-CSF gene within either autologous or allogeneic tumor cell populations has demonstrated evidence of immune stimulation in patients and evidence of antitumor activity particularly in prostate cancer and non–small-cell lung cancer. Results of preclinical studies justify clinical investigation. A summary of clinical results is presented.

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## PEDIATRIC BLOOD AND CANCER

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### Robotically guided radiosurgery for children

Giller CA, Berger BD, Pistenmaa DA, Sklar F, Weprin B, Shapiro K, Winick N, Mulne AF, Delp JL, Gilio JP, Gall KP, Dicke KA, Swift D, Sacco D, Harris-Henderson K, Bowers D

*Pediatr Blood Cancer* 2005;45(3):304–310. Copyright 2004, Wiley-Liss Inc. Reprinted with permission of Wiley-Liss Inc., a subsidiary of John Wiley & Sons Inc.

**Background:** A robotically guided linear accelerator has recently been developed which provides frameless radiosurgery with high precision. Potential advantages for the pediatric population include the avoidance of the cognitive decline associated with whole brain radiotherapy, the ability to treat young children with thin skulls unsuitable for frame-based methods, and the possible avoidance of general anesthesia. We report our experience with this system (the “Cyberknife”) in the treatment of 21 children.

**Procedures:** Cyberknife radiosurgery was performed on 38 occasions for 21 patients, age ranging from 8 months to 16 years ( $7.0 \pm 5.1$  years), with tumors considered unresectable. Three had pilocytic astrocytomas, two had anaplastic astrocytomas, three had ependymomas (two anaplastic), four had medulloblastomas, three had atypical teratoid/rhabdoid tumors, three had craniopharyngiomas, and three had other pathologies. The mean target volume was  $10.7 \pm 20$  cm<sup>3</sup>, mean marginal dose was  $18.8 \pm 8.1$  Gy, and mean follow-up is  $18 \pm 11$  months. Twenty-seven (71%) of the treatments were single-shot and eight (38%) patients did not require general anesthesia.

**Results:** Local control was achieved in the patients with pilocytic and anaplastic astrocytoma, three of the patients with medulloblastoma, and the three with craniopharyngioma, but not for those with ependymoma. Two of the patients with rhabdoid tumors are alive 16 and 35 months after this diagnosis. There have been no procedure related deaths or complications.

**Conclusion:** Cyberknife radiosurgery can be used to achieve local control for some children with CNS tumors without the need for rigid head fixation.

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