
Selected published abstracts of Baylor researchers

AMERICAN JOURNAL OF KIDNEY DISEASES

West Nile virus encephalitis in a renal transplant recipient: the role of intravenous immunoglobulin

Saquib R, Randall H, Chandrakantan A, Spak CW, Barri YM

Am J Kidney Dis 2008;52(5):e19–21. Reprinted with permission from Elsevier.

West Nile virus is a common viral infection in endemic areas. Although the disease has a benign course in immunocompetent individuals, it tends to run a more malignant course in immunocompromised patients such as solid-organ transplant recipients. In this study, a renal transplant recipient presented with fever, impaired speech, obtundation, and features suggestive of meningitis on cerebrospinal fluid examination. Although initial serological study results were negative, the patient was treated promptly with intravenous immunoglobulin (IVIG) based on a strong clinical suspicion of West Nile virus encephalitis. Therapy with IVIG was associated with complete recovery of neurological features, and the patient was discharged on day 7 after resolution of neurological complications. The favorable outcome of this patient may be related to early treatment with IVIG.

AMERICAN JOURNAL OF MEDICAL QUALITY

Accelerating Best Care in Pennsylvania: adapting a large academic system's quality improvement process to rural community hospitals

Haydar Z, Gunderson J, Ballard DJ, Skoufalos A, Berman B, Nash DB

Am J Med Qual 2008;23(4):252–258. Copyright © 2008 by the American College of Medical Quality. Reprinted by permission of SAGE Publications.

Industrial quality improvement (QI) methods such as continuous quality improvement (CQI) may help bridge the gap between evidence-based “best care” and the quality of care provided. In 2006, Baylor Health Care System collaborated with Jefferson Medical College of Thomas Jefferson University to conduct a QI demonstration project in select Pennsylvania hospitals using CQI techniques developed by Baylor. The training was provided over a 6-month period and focused on methods for rapid-cycle improvement; data system design; data management; tools to improve patient outcomes, processes of care, and cost-effectiveness; use of clinical guidelines and protocols; leadership skills; and customer service skills. Participants successfully implemented a variety of QI projects. QI education programs developed and pioneered within large health care systems can be adapted and applied successfully to other settings, providing needed tools to smaller rural and community hospitals that lack the necessary resources to establish such programs independently.

AORN JOURNAL

Standardization of a surgical site precleansing technique for vascular patients

Grelle K, Linker L, Maninang J, Bruce S, Vish N, Sample S

AORN J 2008;88(2):261–265. Reprinted with permission from Elsevier.

Surgical site infection (SSI) is a serious complication that can increase hospital costs and length of stay and may be life threatening. The preoperative chlorhexidine shower is widely recommended to decrease SSI risk, although standardized guidelines for this practice and supporting clinical evidence are lacking. Because vascular patients often have comorbidities that hinder preoperative showering, OR nurses at a specialty hospital in Dallas, Texas, developed and implemented an intraoperative surgical site precleansing technique as standard practice for patients undergoing procedures involving the axilla or groin.

CLINICAL CANCER RESEARCH

JCV virus infection in colorectal neoplasia that develops after liver transplantation

Selgrad M, Koornstra JJ, Fini L, Blom M, Huang R, Devol EB, Boersma-van Ek W, Dijkstra G, Verdonk RC, de Jong S, Goel A, Williams SL, Meyer RL, Haagsma EB, Ricciardiello L, Boland GR

Clin Cancer Res 2008;14(20):6717–6721. Reprinted with permission from the American Association for Cancer Research.

Purpose: Liver transplant recipients (LTRs) have an increased risk of colorectal neoplasia. The mechanism responsible for this is unknown. JCV encodes for TAg and has been implicated in colorectal carcinogenesis. We hypothesized that the use of immunosuppression in LTRs facilitates activation of JCV and is responsible for the increased risk of neoplasia.

Experimental design: JCV TAg DNA and protein expression were determined in normal colonic epithelium ($n = 15$) and adenomatous polyps ($n = 26$) from LTRs and compared with tissue samples from control patients (normal colon, $n = 21$; adenomas, $n = 40$). Apoptosis and proliferation were determined by M30 and Ki-67 immunoreactivity, respectively.

Results: JCV TAg DNA was found in 10 of 15 (67%) of normal colonic mucosa from LTRs compared with 5 of 21 (24%) of control normal mucosa ($P = 0.025$). JCV TAg DNA was detected in 16 of 26 (62%) of the adenomas from LTRs and in 20 of 40 (50%) of control adenomas. JCV TAg protein was expressed in 13 of 26 (50%) adenomas from LTRs versus 2 of 40 (5%) of adenomas from controls ($P < 0.001$). In adenomas from LTRs, the mean proliferative activity was higher compared with controls ($60.3 \pm 3.2\%$ versus $42.7 \pm 2.8\%$, $P < 0.001$), whereas mean apoptotic indices were lower in LTRs ($0.29 \pm 0.08\%$ versus $0.39 \pm 0.06\%$, $P = 0.05$).

Conclusions: The presence of JCV in the colorectal mucosa and adenomas from LTRs, in concert with the use of immunosuppressive agents, suggests that JCV may undergo reactivation, and the subsequent TAG protein expression might explain the increased risk of colorectal neoplasia in LTRs.

CUTIS

One-week treatment with once-daily fluorouracil cream 0.5% in participants with actinic keratoses

Menter A, Vamvakias G, Jorizzo J

Cutis 2008;81(6):509–516. Reprinted with permission.

Actinic keratoses (AKs) are common in fair-skinned individuals with a history of chronic and excessive sun exposure and may progress to squamous cell carcinoma (SCC). Topical fluorouracil is an effective therapeutic option for patients with AKs, but it is associated with substantial skin irritation. The efficacy and tolerability of 1-week treatment using microsphere-based fluorouracil cream 0.5% were analyzed in 356 participants with AK lesions. One-week treatment with once-daily fluorouracil cream 0.5% was significantly more effective than vehicle control in reducing AK lesions and in achieving complete clearance ($P < .001$). No serious treatment-related adverse events occurred. The most frequent treatment-related adverse events were facial and eye irritations, which were predominantly mild to moderate in severity. No participants in the fluorouracil cream 0.5% treatment group discontinued the study because of treatment-related adverse events. One-week treatment with once-daily fluorouracil cream 0.5% is an effective well-tolerated therapy for AKs. Using this short treatment duration period in combination with cryosurgery may prove beneficial in clinical practice. Extending treatment for up to 4 weeks will further improve AK lesion clearance rates.

GASTROENTEROLOGY

Ascitic fluid lactoferrin for diagnosis of spontaneous bacterial peritonitis

Parsi MA, Saadeh SN, Zein NN, Davis GL, Lopez R, Boone J, Lepe MR, Guo L, Ashfaq M, Klintmalm G, McCullough AJ

Gastroenterology 2008;135(3):803–807. Reprinted with permission from Elsevier.

Background and aims: The diagnosis of spontaneous bacterial peritonitis (SBP) is based on a manual count of ascitic fluid polymorphonuclear cells (PMNs). This procedure is operator-dependent and lysis of PMNs during transport to the laboratory may lead to false-negative results. Furthermore, ascitic fluid culture is insensitive and leads to delays in diagnosis. The aim of this study was to assess the utility of ascitic fluid lactoferrin (AFLAC) for the diagnosis of SBP and to identify a cut-off level that can be used for future development of a rapid bedside test.

Methods: A total of 218 consecutive ascites samples from 148 patients (1–8 samples per patient) with cirrhosis at 2 tertiary care medical centers were examined for PMN count, bedside culture, and lactoferrin concentration. AFLAC concentrations were determined using a polyclonal antibody-based enzyme-linked immunosorbent assay. An ascitic fluid PMN count of 250 cells/mL or greater with or without a positive culture was used for diagnosis of SBP.

Results: Twenty-two (10.1%) samples fulfilled diagnostic criteria for SBP. Samples with SBP had a significantly higher lactoferrin concentration (median, 3744 ng/mL; 25th–75th percentiles [P25–P75], 788–9617) compared with non-SBP samples (median, 31 ng/mL; P25–P75, 12–67; $P < .001$). By using a cut-off level of 242 ng/mL, the sensitivity and specificity of the assay for diagnosis of SBP were 95.5% and 97%, respectively. The area under the receiver operating characteristic curve was 0.98.

Conclusions: AFLAC can serve as a sensitive and specific test for diagnosis of SBP. Qualitative bedside assays for the measurement of AFLAC can be developed easily and may serve as a rapid and reliable screening tool for SBP in patients with cirrhosis.

GASTROINTESTINAL ENDOSCOPY CLINICS OF NORTH AMERICA

Intraductal papillary mucinous neoplasms

Burdick JS

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Intraductal papillary mucinous neoplasm (IPMN) is characterized by enhanced mucus secretion. It is a benign or low-grade neoplasm associated with a dilated main pancreatic duct, patulous ampullary orifice, and abundant mucus secretion. Foci of aggressive cancer may arise and become invasive. Surgery is the only treatment that can cure IPMN, but the extent of pancreatic resection and the intraoperative margins remain areas of controversy. The risks of total pancreatectomy must be weighed against the risk for developing cancer in the residual pancreas. Risks must be factored against the natural course of the disease and the likelihood of malignancy developing over the life expectancy.

The molecular biology of gastrointestinal cancer: implications for diagnosis and therapy

Boland CR

Gastrointest Endosc Clin N Am 2008;18(3):401–413. Reprinted with permission from Elsevier.

Cancers are caused by the sequential accumulation of alterations in genes that control the growth, differentiation, and other behaviors of cells. It has long been recognized that cancers are very heterogeneous pathologically, which is a reflection of the variable genetic lesions that give rise to the variety of lesions present in the gastrointestinal tract. Despite this complexity, certain types of genetic alterations are linked to specific pathologic lesions. This review summarizes the current understanding of the molecular pathogenesis of gastrointestinal neoplasia and provides explanations for some of the pathologic variability of lesions encountered by the endoscopist.

IMMUNITY

Functional specializations of human epidermal Langerhans cells and CD14⁺ dermal dendritic cells

Klechevsky E, Morita R, Liu M, Cao Y, Coquery S, Thompson-Snipes L, Briere F, Chaussabel D, Zurawski G, Palucka AK, Reiter Y, Banchereau J, Ueno H

Immunity 2008;29(3):497–510. Reprinted with permission from Elsevier.

Little is known about the functional differences between the human skin myeloid dendritic cell (DC) subsets, epidermal CD207⁺ Langerhans cells (LCs) and dermal CD14⁺ DCs. We showed that CD14⁺ DCs primed CD4⁺ T cells into cells that induce naive B cells to switch isotype and become plasma cells. In contrast, LCs preferentially induced the differentiation of CD4⁺ T cells secreting T helper 2 (Th2) cell cytokines and were efficient at priming and crosspriming naive CD8⁺ T cells. A third DC population, CD14⁺-CD207⁻-CD1a⁺ DC, which resides in the dermis, could activate CD8⁺ T cells better than CD14⁺ DCs but less efficiently than LCs. Thus, the human skin displays three DC subsets, two of which, i.e., CD14⁺ DCs and LCs, display functional specializations, the preferential activation of humoral and cellular immunity, respectively.

A modular analysis framework for blood genomics studies: application to systemic lupus erythematosus

Chaussabel D, Quinn C, Shen J, Patel P, Glaser C, Baldwin N, Stichweh D, Blankenship D, Li L, Munagala I, Bennett L, Allantaz F, Mejias A, Ardura M, Kaizer E, Monnet L, Allman W, Randall H, Johnson D, Lanier A, Punaro M, Wittkowski KM, White P, Fay J, Klintmalm G, Ramilo O, Palucka AK, Banchereau J, Pascual V

Immunity 2008;29(1):150–164. Reprinted with permission from Elsevier.

The analysis of patient blood transcriptional profiles offers a means to investigate the immunological mechanisms relevant to human diseases on a genome-wide scale. In addition, such studies provide a basis for the discovery of clinically relevant biomarker signatures. We designed a strategy for microarray analysis that is based on the identification of transcriptional modules formed by genes coordinately expressed in multiple disease data sets. Mapping changes in gene expression at the module level generated disease-specific transcriptional fingerprints that provide a stable framework for the visualization and functional interpretation of microarray data. These transcriptional modules were used as a basis for the selection of biomarkers and the development of a multivariate transcriptional indicator of disease progression in

patients with systemic lupus erythematosus. Thus, this work describes the implementation and application of a methodology designed to support systems-scale analysis of the human immune system in translational research settings.

NEUROLOGY

Carnitine palmitoyltransferase II deficiency: successful anaplerotic diet therapy

Roe CR, Yang BZ, Brunengraber H, Roe DS, Wallace M, Garritson BK

Neurology 2008;71(4):260–264. Reprinted with permission from Lippincott Williams & Wilkins.

Background: Carnitine palmitoyltransferase II (CPT II) deficiency is an important cause of recurrent rhabdomyolysis in children and adults. Current treatment includes dietary fat restriction, with increased carbohydrate intake and exercise restriction to avoid muscle pain and rhabdomyolysis.

Methods: CPT II enzyme assay, DNA mutation analysis, quantitative analysis of acylcarnitines in blood and cultured fibroblasts, urinary organic acids, the standardized 36-item Short-Form Health Status survey (SF-36) version 2, and bioelectric impedance for body fat composition. Diet treatment with triheptanoin at 30% to 35% of total daily caloric intake was used for all patients.

Results: Seven patients with CPT II deficiency were studied from 7 to 61 months on the triheptanoin (anaplerotic) diet. Five had previous episodes of rhabdomyolysis requiring hospitalizations and muscle pain on exertion prior to the diet (two younger patients had not had rhabdomyolysis). While on the diet, only two patients experienced mild muscle pain with exercise. During short periods of noncompliance, two patients experienced rhabdomyolysis with exercise. None experienced rhabdomyolysis or hospitalizations while on the diet. All patients returned to normal physical activities including strenuous sports. Exercise restriction was eliminated. Previously abnormal SF-36 physical composite scores returned to normal levels that persisted for the duration of the therapy in all five symptomatic patients.

Conclusions: The triheptanoin diet seems to be an effective therapy for adult-onset carnitine palmitoyltransferase II deficiency.

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