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# Selected published abstracts of Baylor researchers

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## AMERICAN JOURNAL OF CARDIOLOGY

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### Validation of the i-STAT handheld activated clotting time for use with bivalirudin

Schussler JM, Lander SR, Wissinger LA, Anwar A, Donsky MS, Johnson KB, Vallabhan RC, Wischmeyer JB

(*Am J Cardiol* 2004;93:1318–1319) Reprinted with permission from Excerpta Medica, Inc.

Bivalirudin is being used more frequently as an anticoagulant in the cardiac catheterization laboratory. Newer devices, used to measure activated clotting time (ACT), have not been thoroughly tested for use with bivalirudin. One such device, the i-STAT ACT, measures the generation of activated thrombin to determine the level of anticoagulation. Our study demonstrated a high level of agreement between the i-STAT ACT and the Hemochron ACT in patients anticoagulated with bivalirudin. In addition, the i-STAT was shown to have an extremely high degree of reproducibility.

## AMERICAN JOURNAL OF MEDICINE

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### The relation of autopsy rate to physicians' beliefs and recommendations regarding autopsy

Burton EC, Phillips RS, Covinsky KE, Sands LP, Goldman L, Dawson NV, Connors AF Jr, Landefeld CS

(*Am J Med* 2004;117:255–261) Reprinted with permission from Excerpta Medica, Inc.

*Purpose:* Multiple factors have affected the decline in autopsy rates. Our goal was to determine the relation of physicians' recommendations regarding autopsy, as well as patient and surrogate decision-maker characteristics, to autopsy performance.

*Methods:* We assessed measures related to autopsy performance using data from two teaching institutions in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. We included patients who had died within 6 months of their index hospitalization and for whom information was available on autopsy performance, physicians' response to questions about autopsy, and interviews with surrogate decision makers about autopsy performance. We assessed the association between autopsy performance and the strength of a physician's recommendation for autopsy, adjusting for patient, surrogate, and physician characteristics.

*Results:* Of the 680 patients who died, 59% ( $n = 402$ ) met our inclusion criteria. Based on physician and surrogate responses, the expected autopsy rate was 42% while the actual autopsy rate was 23%. The autopsy rate was higher when the physician's recommendation for autopsy was strong or very strong at the time of death compared with when autopsy was not recommended strongly or not at all ( $P < 0.001$ ). The strength of the physician's postmortem recommendation was independently associated with autopsy performance after adjusting for patient, surrogate, and physician characteristics ( $P < 0.001$ ).

*Conclusion:* Autopsies are less likely to be performed when not recommended strongly or not at all. Training physicians (or others) how to recommend autopsies may increase autopsy rates.

## ARCHIVES OF INTERNAL MEDICINE

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### Fatal mesenteric fibromuscular dysplasia: a case report and review of the literature

Guill CK, Benavides DC, Rees C, Fennes AZ, Burton EC

(*Arch Intern Med* 2004;164:1148–1153) Copyright © 2004, American Medical Association. All rights reserved.

Fibromuscular dysplasia is a rare nonatherosclerotic, noninflammatory angiopathy of uncertain etiology and high morbidity. Because of its propensity to affect medium-sized vessels in a variety of locations, presenting symptoms may vary substantially, resulting in a delayed or missed diagnosis. We describe a 57-year-old woman who, on multiple occasions, presented with progressive gastrointestinal symptoms and eventually underwent surgical revascularization for celiac and superior mesenteric artery stenosis of uncertain etiology. Her postoperative course was complicated by bowel ischemia, multiple organ failure, and death. Autopsy findings proved useful in determining the underlying disease process and cause of death. This case report and a review of the literature illustrate the high morbidity and mortality that are caused by mesenteric fibromuscular dysplasia, the challenge in establishing a correct diagnosis, and the importance of early detection and treatment.

## GASTROENTEROLOGY

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### Inhibition of neutral sodium absorption by a prostaglandin analogue in patients with cystic fibrosis

Coates SW Jr, Högenauer C, Santa Ana CA, Rosenblatt RL, Emmett M, Fordtran JS

(*Gastroenterology* 2004;127:65–72) Copyright © 2004. Reprinted with permission from the American Gastroenterological Association.

*Background and aims:* In normal intestine, cyclic nucleotides (adenosine 3',5'-cyclic monophosphate [cAMP], guanosine 3',5'-cyclic monophosphate) and  $Ca^{2+}$  inhibit neutral sodium absorption. In contrast, in the jejunum of a knockout mouse model of cystic fibrosis (CF), agents that elevate intracellular cAMP levels did not inhibit neutral sodium absorption, suggesting that the antiabsorptive effect of cAMP is dependent on the cystic fibrosis transmembrane conductance regulator (CFTR). The aim of the present study was to determine if a prostaglandin  $E_1$  analogue, which causes elevation of intracellular cAMP and  $Ca^{2+}$  levels, inhibits neutral sodium absorption in patients with CF in vivo.

*Methods:* Electrolyte and water absorption/secretion was measured during steady-state perfusion of the jejunum with a balanced electrolyte solution. Patients with CF and healthy subjects were studied under basal conditions and during intraluminal infusion of a prostaglandin  $E_1$  analogue (misoprostol).

*Results:* The rate of neutral sodium absorption in the basal state was similar in healthy subjects and patients with CF. Prostaglandin infusion markedly reduced neutral sodium absorption in both healthy subjects and patients with CF. Prostaglandin caused high rates of electrolyte and water secretion in healthy subjects but only trivial rates of secretion in patients with CF.

*Conclusions:* CFTR mutations causing CF in humans do not prevent prostaglandin  $E_1$  inhibition of neutral sodium absorption, even though these mutations produce a severe defect in prostaglandin-stimulated electrolyte secretion. These findings suggest that an intact antiabsorptive

response to either cAMP or  $Ca^{2+}$  may contribute to the relatively low level of intestinal disease in patients with CF.

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## IMMUNITY

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### Autoimmunity through cytokine-induced dendritic cell activation

Banchereau J, Pascual V, Palucka AK

(*Immunity* 2004;20:539–550) Reprinted with permission from Elsevier.

We propose a model where autoimmunity can be viewed as a dynamic system driven by opposite vectors IFN- $\alpha/\beta$  and TNF. These cytokines drive differentiation of distinct types of DCs, TNF-DCs, or IFN-DCs, which present different antigens leading to distinct autoimmune responses. When balanced, both cytokines synergize in protective immunity. When one of the cytokines prevails, autoimmunity occurs, Type I interferons (IFN- $\alpha/\beta$ ) playing a major role in systemic lupus erythematosus (SLE) and TNF playing a major role in rheumatoid arthritis. This model complements the Type 1/Type 2 paradigm. Therefore, immunity can be viewed as a dynamic system driven by two sets of opposite vectors: IFN- $\alpha/\beta$ /TNF and IFN- $\gamma$ /IL-4.

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## JOURNAL OF THE AMERICAN GERIATRIC SOCIETY

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### Differences in end-of-life preferences between congestive heart failure and dementia in a medical house calls program

Haydar ZR, Lowe AJ, Kahveci KL, Weatherford W, Finucane T

(*J Am Geriatr Soc* 2004;52:736–740) Reprinted with permission from Blackwell Publishing.

**Objectives:** To compare end-of-life preferences in elderly individuals with dementia and congestive heart failure (CHF).

**Design:** Retrospective case-control study.

**Setting:** Geriatrician-led interdisciplinary house-call program using an electronic medical record.

**Participants:** Homebound individuals who died while under the care of the house-call program from October 1996 to April 2001.

**Measurements:** Medical records review for demographics, functional status, advance medical planning, hospice use, and place of death.

**Results:** Of 172 patients who died in the program, 29 had CHF, 79 had dementia, 34 had both, and 30 had neither. Patients with CHF were younger (82.6 vs 87.0,  $P = 0.011$ ) and less functionally dependent (activities of daily living score 9.1 vs 11.5,  $P = 0.001$ ). Time from enrollment to death was not significantly different (mean  $\pm$  standard deviation =  $444 \pm 375$  days for CHF vs  $325 \pm 330$  days for dementia,  $P = 0.113$ ). A do-not-resuscitate (DNR) directive was given in 62% of patients with CHF and 91% with dementia ( $P < 0.001$ ). Advance medical planning discussions were not significantly different (2.10 in CHF vs 1.65 in dementia,  $P = 0.100$ ). More patients with CHF participated in their advance medical planning than those with dementia (86% vs 17%,  $P < 0.001$ ). Hospice was used in 24% of CHF and 61% of dementia cases ( $P < 0.001$ ). Finally, 45% of patients with CHF and 18% of patients with dementia died in the acute hospital ( $P = 0.006$ ). Multivariate analysis showed that the fact that more patients with CHF were involved in their medical planning was not significant in predicting end-of-life preferences. Alternatively, Caucasian ethnicity was an independent predictor of having a documented DNR and death outside of the acute hospital.

**Conclusion:** In the months before death, patients with CHF were more likely to have care plans directed at disease modification and treatment, whereas dementia patients were more likely to have care plans that focused on symptom relief and anticipation of dying. Several factors may contribute to this difference.

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## JOURNAL OF CLINICAL GASTROENTEROLOGY

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### Diagnosis and management of microscopic colitis syndrome

Schiller LR

(*J Clin Gastroenterol* 2004;38[5 Suppl]:S27–S30)

Microscopic colitis syndrome consists of chronic watery diarrhea, a normal or near-normal gross appearance of the colonic mucosa, and a specific histologic picture described as either lymphocytic colitis or collagenous colitis. The cause of microscopic colitis is unknown, but recent work suggests some immunologic similarities to celiac disease, suggesting that luminal antigens may be important in its pathogenesis. Diarrhea in microscopic colitis seems to be directly related to the extent of inflammation, suggesting that inflammatory mediators are responsible for reduced water absorption by the colon. Microscopic colitis is a frequent diagnosis in patients with chronic diarrhea seen at referral centers. It is often associated with other immune-mediated conditions and frequently is complicated by fecal incontinence. The differential diagnosis is broad, comprising all causes of watery diarrhea. Evaluation is straightforward with the key aspect being review of colon biopsy specimens by an experienced pathologist. Treatment is still being defined: symptomatic management with antidiarrheal agents, 5-aminosalicylate drugs, corticosteroids, especially budesonide, bile acid-binding resins, and bismuth subsalicylate all can be effective. The prognosis is good with no evidence of conversion to classic inflammatory bowel disease or of development of neoplasia over time.

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## JOURNAL OF INHERITED METABOLIC DISEASE

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### Tetrahydrobiopterin deficiency and dopamine loss in a genetic mouse model of Lesch-Nyhan disease

Hyland K, Kasim S, Egami K, Arnold LA, Jinnah HA

(*J Inherit Metab Dis* 2004;27:165–178; <http://www.kluweronline.com/issn/0141-8955>) Reprinted with kind permission of Springer Science and Business Media.

Hypoxanthine-guanine phosphoribosyltransferase (HPRT) is an enzyme that catalyses the conversion of hypoxanthine and guanine into their respective nucleotides. Inherited deficiency of the enzyme is associated with a loss of striatal dopamine in both mouse and man. Although HPRT is not directly involved in the metabolism of dopamine, it contributes to the supply of GTP, which is used in the first and rate-limiting step in the synthesis of tetrahydrobiopterin ( $BH_4$ ). Since  $BH_4$  is required as a cofactor for tyrosine hydroxylase in the synthesis of dopamine, any limitation in the supply of GTP could interfere with the synthesis of dopamine. The current studies were designed to address the hypothesis that the reduced striatal dopamine in mice with HPRT deficiency results from reduced availability of  $BH_4$ . The mutant mice had small reductions in striatal  $BH_4$ , with normal  $BH_4$  levels in other brain regions. Liver  $BH_4$  was normal in HPRT-deficient mutant mice, and a phenylalanine challenge test failed to reveal any evidence for impaired hepatic phenylalanine hydroxylase, another  $BH_4$ -dependent enzyme. Although striatal  $BH_4$  content is not normal, supplementation with  $BH_4$  or L-dopa failed to correct the striatal dopamine deficiency of the mutant mice, suggesting that  $BH_4$  limitation is not responsible for the dopamine loss.

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