UTSW Internal Medicine Journal Watch (November 2014)

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Physiological Approach to Assessment of Acid–Base Disturbances


**Commentary:**

Maintaining equilibrium in the acid-base system is crucial for the normal functioning of the human body. The ability to discern the presence of disturbances in this system and the underlying physiology leading to these disturbances is essential for effective management and more importantly, helps you survive your MICU rotations. This review provides an approach on how to analyze and interpret different acid-base disorder in a stepwise fashion and gives three different case examples on how to do it.

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Infectious Diseases

Clinical Management of Staphylococcus Aureus Bacteremia: A review.

Commentary:
This systematic review by experts in the field from Duke summarizes the existing literature on two important clinical management questions related to Staphylococcus aureus bacteremia: 1) Is TEE required in all patients? 2) What is the best treatment for MRSA bacteremia? The bottom line conclusions were that most patients need a transesophageal echocardiogram to exclude endocarditis, with the exception of a small subset of patients who meet all of the following specific criteria: absence of cardiac device or secondary foci of infection, nosocomial acquisition, clearance of bacteremia within 4 days, no hemodialysis, and no clinical evidence of infective endocarditis. With regards to treatment, the literature overall is lacking but vancomycin or daptomycin are the first-line options for MRSA bacteremia.

*Link via UTSW*

Drugs for MRSA Skin and Soft-Tissue Infections.
*Dr. Nicolas Barros reviewing JAMA 2014; 312(15): 1583-84.*

Commentary:
This brief summary from the Medical Letter section is a useful reference for reviewing basic information about MRSA skin infections and dosing of available oral and intravenous drugs with activity against MRSA.

*Link via UTSW*
Review: Community Acquired Pneumonia.


Commentary:

This NEJM review nicely summarizes the major considerations regarding the microbiology and treatment of community-acquired pneumonia. In particular, the discussion surrounding duration of treatment (5-7 days only for outpatients or inpatients who respond promptly to therapy) and a more nuanced approach to empiric therapy is worth close attention.

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Hepatocellular carcinoma (HCC) is the fastest-rising cause of cancer-related deaths in the United States, where hepatitis C virus (HCV) is the major underlying etiology for HCC. Survival with HCC is dismal (5-year survival rate is approximately 10%). Serum levels of α-fetoprotein (AFP) and liver ultrasonography are used for screening of HCC. However, the levels of AFP are influenced not only by the presence of HCC, but also by the underlying severity and activity of liver disease, which is reflected by platelet count and liver function tests. In the recent issue of Gastroenterology, El-Serag et al. constructed an AFP-based algorithm that included additional factors to identify patients at risk for HCC. The authors tested the predictive ability of this algorithm in a large retrospective dataset of patients with HCC with underlying HCV cirrhosis using nation-wide dataset from the VA system involving 12,000 patients. The study has shown that at any given AFP value, low platelet count, low ALT and older age were associated with increased risk of HCC. In contrast, high levels of ALT and normal/high numbers of platelets were associated with lower risk for HCC (See attached Figure on the next page). In summary, the report introduces a novel predictive model using AFP, platelets, ALT and age that significantly enhances the predictive value of AFP for detecting HCC. However, it is unknown whether the predictive characteristics of this model are influenced by HCV treatment (this information was not included in the manuscript) and whether this algorithm can be extrapolated to other liver diseases.

[Link via UTSW]
**Figure:** Contour plot showing HCC probability at AFP level of 20 ng/mL as calculated from a predictive model containing AFP, age, ALT, and platelets. HCC probability at age 50 years (fixed) varies considerably over a range of ALT and platelets values. HCC probabilities are depicted in different colors.

**Guidelines: New HCV Drugs Should Go to Sickest Patients**


**Brief Summary:** Patients with compensated HCV cirrhosis, HCV-related liver transplant or with extrahepatic symptoms of HCV should be first in line for treatment.

**Commentary:**

A recent review of cost-effectiveness of new HCV therapies, including Sofosbuvir, raised important questions about the value of these drugs to patients and the health system. Optimally,
all patients with chronic HCV should be treated. However, in light of the costs ($81,000 per treatment), public and private insurers face unbearable costs and will be forced to develop stringent eligibility criteria to manage the tension between access and affordability. This has been reflected in the recent update of the AASLD/IDSA guidelines on HCV treatment based on which the highest priority is assigned to patients with advanced fibrosis (Metavir F3), patients with compensated cirrhosis (Metavir F4), liver transplant recipients, and patients with severe extrahepatic hepatitis C. Ongoing assessment of liver disease is recommend for patients in whom therapy is deferred, such as HCV patients without fibrosis or cirrhosis.
Critical Care

Lower vs. Higher Hemoglobin Threshold for Transfusion in Septic shock


Brief Summary: Is there a goal Hemoglobin value to transfuse in Septic shock? The results of this study suggest no statistical difference in 30 day mortality and numerous secondary outcomes when patients with sepsis were transfused to a goal of 7 g/dL vs. 9 g/dL.

Commentary:

The surviving Sepsis Campaign recommendations regarding transfusions in septic shock include transfusion to maintain a hematocrit>30% in the first 6 hours of presentation for patients with a central venous sat less than 70%. After that, they recommend aiming for a goal of 7-9 g/dL with transfusion for less than 7. These recommendations have limited date supporting them. Recent studies such as the FOCUS trial (Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair) and a Cochrane meta-analysis suggested using restrictive transfusion protocols. This hypothesis was tested in a multicenter, European partially blind, randomized trial that compared death at 90 days in patients with septic shock in patient who were transfused to a Hg goal of 7 (lower threshold) vs. those transfused to a Hg goal of 9(higher threshold). At 90 days, there were no significant differences found in mortality, use of life support, serious adverse reactions, ischemic events (Myocardial infarction, intestinal ischemia, and limb ischemia), percent of days without vasopressor therapy, mechanical ventilation, or renal-replacement therapy. These results were even seen in patients with chronic cardiovascular disease, older age, and greater disease severity.

This may not hold true in patients with acute MIs, and some of these results may be related to the fact that all patients were given leukoreduced blood, regardless of cancer status. Overall the findings of this study are in accordance with recent literature that transfusion to a lower threshold vs. that of a higher threshold is not associated with any statistically significant differences in the majority of patients with septic shock.

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Geriatrics

Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults


Brief Summary: In adults greater than 65 years of age, high-dose influenza vaccine may provide better protection against the influenza virus when compared to standard dosing.

Commentary:

Previous studies have shown that when compared to standard dose (SD) influenza vaccines, the trivalent, high dose (HD) inactivated vaccine increases antibody responses to the influenza virus in patients 65 and older. This large multicenter, randomized double blind study aimed to assess relative efficacy, safety and immunogenicity of the HD to the SD vaccine in older adults. After vaccination, titers and seroprotection rates were shown to be higher in the HD group. The overall efficacy of the HD vaccine indicated that roughly one quarter of all breakthrough illnesses could potentially be prevented if the HD vaccine was used instead of SD. The relative safety in conjunction with the effectiveness analyses in this study suggests favorable effects of the HD vaccine on prevention of pneumonia, hospitalizations, medication use and non-routine medical visits. However when examining the absolute numbers and calculating the number needed to treat, the results may not be as robust as quoted in the study.

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Nephrology

CKD and the Risk of Incident Cancer

*Dr. Benjamin Jenny reviewing Lowrance, et al. JASN October 2014 25: 2327-2334; published ahead of print May 29, 2014*

Commentary:

This retrospective cohort study analyzed 1,190,538 patients in the California Kaiser Permanente health care system to explore the association between glomerular filtration rate (GFR) and the subsequent development of cancer. Renal cancer (primary outcome) as well as urothelial, prostate, breast, lung and colorectal (secondary outcomes) were specifically examined. Median patient age and length of follow up was 55 and 5.3 years respectively. 76,809 cancers were diagnosed in 72,875 patients during the study period, with renal and urothelial cancers revealing a graded increased risk: renal cancer 0.22 per 1000 person years (GFR = 60-90 ml/min per 1.73 m²), 1.08 per 1000 person years (GFR < 30 ml/min per 1.73 m²); urothelial cancer 0.17 per 1000 person years (GFR = 60-90 ml/min per 1.73 m²) and 0.58 per 1000 person years (GFR < 30 ml/min per 1.73 m²). No progressive increase in incidence was observed in the secondary outcomes. Patients with chronic kidney disease (CKD) are burdened with persistent inflammatory and oxidative stressors along with a degree of immunodeficiency (especially in lower GFR categories) that by description alone appears ideal for the genesis and subsequent development of malignancy. While there are many guidelines for the longitudinal care of patients with CKD, no specific malignancy screening recommendations exist at this time. While further investigation into this association is needed, this article underscores the danger of persistent renal dysfunction on patient longevity.

*Link via UTSW*
Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes


Commentary:

This month we address the impact on mortality, macrovascular, and microvascular events when placing our patients with type 2 diabetes on an ace-inhibitor/thiazide diuretic combination and/or intensively controlling their blood glucose with A1C<6.5%.

This paper reports on a 6-year post-trial up of the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) Study, which lasted about 5 years, and found significant reductions in rates of death from any cause and from cardiovascular causes with fixed dose ACE-inhibitor perindopril (4mg) and thiazide diuretic indapamide (1.25mg) vs. matching placebo. However it did not find significant benefits in mortality, macrovascular, or microvascular events after sulfonylurea gliclazide based intensive glucose control HbA1C<6.5% vs. goal standard glucose control based on local guidelines.

This outcome in glucose control is different from other landmark studies such as DCCT-EDIC (intensive glucose control in type 1 diabetes) or UKPDS (intensive glucose control in newly diagnosed type 2 diabetes) and may be because this study used older patients with established disease, had a relatively short follow-up period, and because the baseline HbA1C in these older studies was much worse (>8.5% vs 7.5% in this study).

In summary, among patients with long-standing type 2 diabetes, blood pressure lowering treatment with perindopril-indapamide for about 4.5 years resulted in significant long-term benefits in death from any cause and cardiovascular causes while intensive glucose control for an average of 5 years failed to reduce mortality or major macrovascular events.

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Cardiology

Thoracic Aortic Aneurysm and Dissection

Dr. Benjamin Jenny reviewing Goldfinger et al. J Am Coll Cardiol. 2014; 64(16):1725-1739

Commentary:

Aortic aneurysm formation complicated by dissection occurs with an annual incidence of between 6 to 16 cases per 100,000. Risk factors for aneurysm formation include medical conditions that lead to medial degeneration of blood vessels (Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome, Familial thoracic aortic aneurysm and dissection syndrome), anatomical abnormalities (bicuspitate aortic valve, aortic coarctation, Turner’s syndrome), inflammatory processes (Takayasu’s arteritis, giant cell arteritis, Behcet’s disease, syphilis), increased aortic wall stress (hypertension, cocaine use, weight lifting, smoking) and pregnancy. There are two classification systems for aortic dissection, the DeBakey and Stanford, which are both based upon the initial location of the dissection (ascending vs. descending aorta). While certain genetic conditions have specific surveillance and intervention parameters, an aortic aneurysm greater than or equal to 5.5 cm or enlarging at a rate of 0.5 cm/year is a class 1 indication for surgical intervention. Finally, while patients with aortic dissection classically present with hypertension, aortic dissection accompanied by hypotension should alert the clinician to investigate proximal dissection complications such as coronary obstruction, aortic insufficiency and cardiac tamponade.

Link via UTSW
EKG solutions

Posterior EKG:
A 65 year-old man with a history of hypertension and diabetes presented to the ED reporting substernal chest pain exacerbated with exertion that was subsequently relieved with sublingual nitroglycerin and morphine. The above EKG was obtained which was notable for sinus tachycardia and ST segment elevation in leads I, AVL and ST segment depression in leads V1- V6. The differential for ST segment elevation includes: ischemia (lateral STEMI), pericarditis, early repolarization, coronary vasospasm, ventricular aneurysm and Takotsubo cardiomyopathy. The differential for ST depression includes: ischemia (true posterior STEMI, NSTEMI, stable or unstable angina, reciprocal change), rate related, strain, digoxin use, hypokalemia and hypomagnesemia.

In this patient, the ST elevation in the lateral leads combined with the ST depression in the anterior leads was concerning for infarction of the circumflex artery resulting in a posterolateral STEMI. A posterior EKG was subsequently obtained which revealed ST segment elevation in leads V8 and V9, indicative of a transmural infarction of the posterior wall of the left ventricle. Posterior MIs should also be considered in all inferior infarctions, as the posterior descending artery arises from the right coronary artery in 85% of the population. In the setting of on-going chest pain and ST segment depression in anterior leads, a posterior EKG can be used to distinguish subendocardial (NSTEMI) from transmural (STEMI) ischemia.