25th ANNUAL
MANAGEMENT OF THE HOSPITALIZED PATIENT
Hyatt Regency San Francisco • San Francisco, CA

Thursday - Saturday
October 21-23, 2021

Praise from past attendees...
“The best conference ever!
By far!!!”

COURSE CHAIR
Robert M. Wachter, MD
Professor and Chair, Department of Medicine
University of California, San Francisco

The course that started it all returns for its 25th year!
This course serves as the West Coast Regional Meeting of
the Society of Hospital Medicine.
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25th Annual
Management of the Hospitalized Patient

October 21 - 23, 2021

Course Chair
Robert M. Wachter, MD
Professor and Chair, Department of Medicine
University of California, San Francisco
Exhibitors

Alexion
Astellas
AstraZeneca
Baylor Scott & White Health
Boehringer Ingelheim
Genentech
Janssen
Theravance
25th Annual Management of the Hospitalized Patient

We are thrilled that you’re joining us for the Management of the Hospitalized Patient CME course

Overview
This course, chaired by Dr. Robert Wachter, covers the clinical issues most relevant to hospitalists and other clinicians who care for inpatients. Taught by UCSF’s top teachers and selected guest faculty, the course – now in its 25th year – highlights recent advances and current controversies. To promote active learning, the course uses a mobile audience response system and features multiple workshops in a variety of disciplines to allow for small group discussions. The course will be offered both in-person and virtually.

The course includes broad content in critical care, perioperative care, patient safety, hospital neurology, cardiology, GI, hematology, oncology, nephrology, and infectious diseases (including Covid).

This course is presented by the UCSF Division of Hospital Medicine and is sponsored by the Office of Continuing Medical Education, University of California, San Francisco School of Medicine. It also serves as the West Coast regional meeting of the Society of Hospital Medicine.

Educational Objectives
An attendee completing the Management of the Hospitalized Patient course should be able to:

- Improve diagnosis of common inpatient clinical presentations;
- Perform an evidence-based work-up for common inpatient clinical presentations;
- Apply modern therapeutic approaches to common inpatient disorders;
- More effectively respond to patients questions in hospital medicine using the latest clinical literature.
The University of California, San Francisco School of Medicine (UCSF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

UCSF designates this educational activity for a maximum of 18.50 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This CME activity meets the requirements under California Assembly Bill 1195, continuing education and cultural and linguistic competency.

**Geriatric Medicine:**
The approved credits shown above include 2.50 Geriatric Credits toward meeting the requirement under California Assembly Bill 1820, Geriatric Medicine.

**ABIM Maintenance of Certification Points:**
Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 18.50 MOC points in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

**Family Physicians:**
The AAFP has reviewed 25th Annual Management of the Hospitalized Patient and deemed it acceptable for up to 18.50 In-Person, Live (could include online) AAFP Prescribed credit. Term of Approval is from 10/21/2021 to 10/23/2021. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Nurses:**
For the purpose of recertification, the American Nurses Credentialing Center accepts AMA PRA Category 1 Credit TM issued by organizations accredited by the ACCME.

**Pharmacotherapeutics CEUs for Nurses:**
This activity is designated for a maximum of 2.50 pharmacotherapeutic credits towards meeting the requirement for nursing pharmacology continuing education. Nurses should claim 0.1 CEUs for each contact hour of participation in designated pharmacotherapeutic continuing education.

**Pharmacists:**
The California Board of Pharmacy accepts as continuing professional education those courses that meet the standard of relevance to pharmacy practice and have been approved for AMA PRA Category 1 Credit™.

**Physician Assistants**
AAPA accepts category 1 credit from AOACCME, Prescribed credit from AAFP, and AMA PRA Category 1 credit™ for organizations accredited by the ACCME.
GENERAL INFORMATION

ATTENDANCE VERIFICATION
Please remember to sign-in on the sign-in sheet when you check in on your first day at the UCSF Registration Desk, located in the Market Street Foyer on the Street Level. *You only need to sign-in once for the course, when you first check in.*

Those attending virtually will be verified upon logging into the Live Stream.

EVALUATIONS / CREDITS / MOC
Visit the MHP Evaluation Site to do all of these things!

Tap the **Evaluation** tile from the app’s home screen. OR Visit [https://tinyurl.com/MHP21Eval](https://tinyurl.com/MHP21Eval) from a web browser.

If asked to login, use the email address and access key you used for the app. *If you didn’t use the mobile app, click the Create Account button.*

Select a “Task” to complete it:
- ✔ Speaker Evaluations
- ✔ Course Evaluation (required for credit)
- ✔ Claim CME / MOC
- ✔ Download Certificate
  - o Print it
  - o Save it as a PDF
  - o Email it
CONTINENTAL BREAKFAST AND COFFEE BREAKS

Breakfasts and coffee breaks provided for the registered attendees will be served in the Grand Ballroom Foyer on the Street Level along with the exhibits and have been ordered according to registration numbers. You name badge will be required to access the exhibitor and meal service area. Guests and travel companions are not permitted.

LUNCH

Lunch is on your own on Thursday 10/21. A list of are restaurants is provided in the MHP2021 app along with a map.

On Friday 10/22, a boxed lunch will be provided. If you have any dietary restrictions that you did not list when you registered, please be sure to let us know as soon as possible so we may prepare accordingly. We will have vegetarian as well as a limited number of vegan and vegan/gluten-free options available. You will have 30 minutes (12:10PM-12:40PM) to collect your boxed lunch before the start of the small group workshop sessions.

COURSE RECEPTION

On Thursday 10/21, we will host the course reception on the east end of the Atrium Lobby located on the Lobby Level and is for registered attendees only. Please make sure to wear your course name badge.

Due to San Francisco Vaccine Verification protocols, we are not able to accommodate guests this year.

GENERAL SESSION

The general session will take place in the Grand Ballroom. We will provide a warning bell during breakfasts and coffee breaks to allow you ample time to re-enter the room before the course reconvenes.
Federal and State Law
Regarding Linguistic Access and Services for Limited English Proficient Persons

I. Purpose.
This document is intended to satisfy the requirements set forth in California Business and Professions code 2190.1. California law requires physicians to obtain training in cultural and linguistic competency as part of their continuing medical education programs. This document and the attachments are intended to provide physicians with an overview of federal and state laws regarding linguistic access and services for limited English proficient (“LEP”) persons. Other federal and state laws not reviewed below also may govern the manner in which physicians and healthcare providers render services for disabled, hearing impaired or other protected categories.

The Federal Civil Rights Act of 1964, as amended, and HHS regulations require recipients of federal financial assistance (“Recipients”) to take reasonable steps to ensure that LEP persons have meaningful access to federally funded programs and services. Failure to provide LEP individuals with access to federally funded programs and services may constitute national origin discrimination, which may be remedied by federal agency enforcement action. Recipients may include physicians, hospitals, universities and academic medical centers who receive grants, training, equipment, surplus property and other assistance from the federal government.

HHS recently issued revised guidance documents for Recipients to ensure that they understand their obligations to provide language assistance services to LEP persons. A copy of HHS’s summary document entitled “Guidance for Federal Financial Assistance Recipients Regarding Title VI and the Prohibition Against National Origin Discrimination Affecting Limited English Proficient Persons – Summary” is available at HHS’s website at: http://www.hhs.gov/ocr/lep/.

As noted above, Recipients generally must provide meaningful access to their programs and services for LEP persons. The rule, however, is a flexible one and HHS recognizes that “reasonable steps” may differ depending on the Recipient’s size and scope of services. HHS advised that Recipients, in designing an LEP program, should conduct an individualized assessment balancing four factors, including: (i) the number or proportion of LEP persons eligible to be served or likely to be encountered by the Recipient; (ii) the frequency with which LEP individuals come into contact with the Recipient’s program; (iii) the nature and importance of the program, activity or service provided by the Recipient to its beneficiaries; and (iv) the resources available to the Recipient and the costs of interpreting and translation services.

Based on the Recipient’s analysis, the Recipient should then design an LEP plan based on five recommended steps, including: (i) identifying LEP individuals who may need assistance; (ii) identifying language assistance measures; (iii) training staff; (iv) providing notice to LEP persons; and (v) monitoring and updating the LEP plan.

A Recipient’s LEP plan likely will include translating vital documents and providing either on-site interpreters or telephone interpreter services, or using shared interpreting services with other Recipients. Recipients may take other reasonable steps depending on the emergent or non-emergent needs of the LEP individual, such as hiring bilingual staff who are competent in the skills required for medical translation, hiring staff interpreters, or contracting with outside public or private agencies that provide interpreter services. HHS’s guidance provides detailed examples of the mix of services that a Recipient should consider and implement.

HHS’s guidance also establishes a “safe harbor” that Recipients may elect to follow when determining whether vital documents must be translated into other languages. Compliance with the safe harbor will be strong evidence that the Recipient has satisfied its written translation obligations.

In addition to reviewing HHS guidance documents, Recipients may contact HHS’s Office for Civil Rights for technical assistance in establishing a reasonable LEP plan.
The California legislature enacted the California’s Dymally-Alatorre Bilingual Services Act (Govt. Code 7290 et seq.) in order to ensure that California residents would appropriately receive services from public agencies regardless of the person’s English language skills. California Government Code section 7291 recites this legislative intent as follows:

“The Legislature hereby finds and declares that the effective maintenance and development of a free and democratic society depends on the right and ability of its citizens and residents to communicate with their government and the right and ability of the government to communicate with them.

The Legislature further finds and declares that substantial numbers of persons who live, work and pay taxes in this state are unable, either because they do not speak or write English at all, or because their primary language is other than English, effectively to communicate with their government. The Legislature further finds and declares that state and local agency employees frequently are unable to communicate with persons requiring their services because of this language barrier. As a consequence, substantial numbers of persons presently are being denied rights and benefits to which they would otherwise be entitled.

It is the intention of the Legislature in enacting this chapter to provide for effective communication between all levels of government in this state and the people of this state who are precluded from utilizing public services because of language barriers.”

The Act generally requires state and local public agencies to provide interpreter and written document translation services in a manner that will ensure that LEP individuals have access to important government services. Agencies may employ bilingual staff, and translate documents into additional languages representing the clientele served by the agency. Public agencies also must conduct a needs assessment survey every two years documenting the items listed in Government Code section 7299.4, and develop an implementation plan every year that documents compliance with the Act. You may access a copy of this law at the following url: http://www.spb.ca.gov/bilingual/dymallyact.htm
## FACULTY LIST

### Course Chair

**Robert M. Wachter, MD**  
Professor and Chair, Department of Medicine  
University of California, San Francisco

### Visiting Faculty

**Linda DeCherrie, MD**  
Professor of Geriatrics and Palliative Medicine; Associate Professor of Medicine, General Internal Medicine,  
Icahn School of Medicine at Mount Sinai, New York, NY

### Course Faculty (University of California, San Francisco, School of Medicine)

**Jennifer Babik, MD, PhD**  
Associate Professor of Medicine, Division of Infectious Diseases; Associate Program Director, Internal Medicine Residency

**Danielle Brandman, MD, MAS**  
Associate Professor of Clinical Medicine; Program Director, Transplant Hepatology Fellowship,  
Division of Gastroenterology/Liver Transplant

**Sam Brondfield, MD, MA**  
Assistant Professor of Medicine, Division of Hematology/Oncology

**H. Quinny Cheng, MD**  
Professor of Medicine; Medical Director, Medicine Consultation Service and Neurosurgery Co-Management Service

**Gurpreet Dhaliwal, MD**  
Professor of Medicine, Medicine Clerkship Site Director, San Francisco VA Health Care System

**Vanja Douglas, MD**  
Associate Professor of Neurology; Sara & Evan Williams Foundation Endowed Neurohospitalist Chair

**Brett M. Eicker, MD**  
Professor of Radiology & Biomedical Imaging; Chief, Cardiac & Pulmonary Imaging

**Monica Gandhi, MD, MPH**  
Professor of Medicine; Associate Division Chief, Division of HIV, Infectious Diseases, and Global Medicine, UCSF/San Francisco General Hospital; Director of the UCSF Center for AIDS Research; Medical Director, HIV Clinic at SFGH

**Sarah Goglin, MD**  
Assistant Professor of Medicine, Department of Rheumatology

**Antonio Gomez, MD**  
Associate Professor of Medicine

**Trevor Jensen, MD, MS**  
Assistant Professor of Medicine, Division of Hospital Medicine

**S. Andrew Josephson, MD**  
Carmen Castro Franceschi and Gladyne K. Mitchell Neurohospitalist Distinguished Professor and Chair, Department of Neurology
Course Faculty (University of California, San Francisco, School of Medicine)

Lowell Lo, MD  
Assistant Professor of Medicine, Division of Nephrology

Gregory M. Marcus, MD  
Professor of Medicine, Division of Cardiology

Marlene Martin, MD  
Associate Professor of Medicine, Division of Hospital Medicine

Tracy Minichiello, MD  
Professor of Medicine; Chief, Anticoagulation and Thrombosis Service,  
San Francisco VA Health Care System

Bradley Monash, MD  
Associate Professor of Medicine and of Pediatrics; Chief of Medicine Service

Craig Munroe, MD  
Associate Professor of Medicine, Division of Gastroenterology; Associate Chief for Clinical Innovation

Erika Price, MD, MPH  
Associate Clinical Professor  
VA Medicine Home, Hospital Medicine, Hospital Medicine VA

George Rutherford, III, MD  
Professor of Epidemiology & Biostatistics  
Director, Prevention and Public Health

Lekshmi Santhosh, MD  
Assistant Professor of Pulmonary and Critical Care Medicine

Anne Schafer, MD  
Associate Professor of Medicine and of Epidemiology & Biostatistics;  
Chief of Endocrinology and Metabolism, San Francisco VA Health Care System

Bradley A. Sharpe, MD  
Professor of Medicine; Chief, Division of Hospital Medicine

Krishan Soni, MD, MBA, FACC  
Assistant Professor, Division of Cardiology
DISCLOSURES

The following faculty speakers, moderators, and planning committee members have disclosed they have no financial interest/arrangement or affiliation with any commercial companies who have provided products or services relating to their presentation(s) or commercial support for this continuing medical education activity:

Jennifer Babik, MD, PhD
H. Quinny Cheng, MD
Linda DeCherrie, MD
Gurpreet Dhaliwal, MD
Vanja Douglas, MD
Brett M. Elicker, MD
Monica Gandhi, MD, MPH
Sarah Goglin, MD
Antonio Gomez, MD
S. Andrew Josephson, MD
Lowell Lo, MD
Marlene Martin, MD
Tracy Minichiello, MD
Bradley Monash, MD
Craig Munroe, MD
Erika Munroe, MD
George Rutherford, III, MD
Lekshmi Santhosh, MD
Bradley A. Sharpe, MD
Krishan Soni, MD

The following faculty speakers have disclosed a financial interest/arrangement or affiliation with a commercial company who has provided products or services relating to their presentation(s) or commercial support for this continuing medical education activity. All conflicts of interest have been resolved in accordance with the ACCME Standards for Commercial Support:

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Company/Institution</th>
<th>Role/Relationship</th>
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<tr>
<td>Danielle Brandman, MD, MAS</td>
<td>Allergan</td>
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<td>Sam Brondfield, MD, MA</td>
<td>Doximity</td>
<td>Honorarium Recipient</td>
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<td>American Physician Institute</td>
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<td>Trevor Jensen, MD</td>
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<td>Baylis Medical</td>
<td>Stock Shareholder (excluding mutual funds)</td>
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<td>Anne Schafer, MD</td>
<td>Amgen</td>
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<td>Robert M. Wachter, MD</td>
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This UCSF CME educational activity was planned and developed to uphold academic standards to ensure balance, independence, objectivity, and scientific rigor; adhere to requirements to protect health information under the Health Insurance Portability and Accountability Act of 1996 (HIPAA); and, include a mechanism to inform learners when unapproved or unlabeled uses of therapeutic products or agents are discussed or referenced.

This activity has been reviewed and approved by members of the UCSF CME Governing Board in accordance with UCSF CME accreditation policies. Office of CME staff, planners, reviewers, and all others in control of content have disclosed no relevant financial relationships.
COURSE PROGRAM

Thursday, October 21, 2021

7:00 AM  Registration and Continental Breakfast

8:00  Welcome and Overview  Robert M. Wachter, MD

8:10  Rx  Diagnosis and Management of VTE in the Hospitalized Patient  Tracy Minichiello, MD

9:00  Update on Clinical Manifestations and Inpatient Management of Covid-19  Jennifer Babik, MD, PhD

9:50  Break

10:15  GRx  Managing Anticoagulation in the Hospitalized Patients  Tracy Minichiello, MD

11:10  GRx  Update in Diagnosis and Management of Stroke  S. Andrew Josephson, MD

12:00 PM  Lunch Break

1:30  Small Group Workshops: Session I

1. The Neurological Exam  S. Andrew Josephson, MD
2. Tough Cases in the Hospitalized Patient with Liver Disease  Danielle Brandman, MD, MAS
3. Thromboembolism Q&A: Cases and Controversies  Tracy Minichiello, MD
4. Tough Cases in Inpatient Pulmonary Medicine  Lekshmi Santhosh, MD
5. Common Hospital Consults in Infectious Disease  Jennifer Babik, MD, PhD
6. Caring for the Hospitalized Patient with Addictions  Marlene Martin, MD
7. Meet the Professor  Robert M. Wachter, MD

2:50  Break

3:15  ICU Management Pearls for the Hospitalist  Lekshmi Santhosh, MD
4:10  Setting Up a Successful Hospital at Home Program  Linda DeCherrie, MD

5:00 PM  Adjourn

P = Pain Credit  G = Geriatric Credit  Rx = Meets Requirements for Pharmacotherapeutics CEUs for NPs/Nurses
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<tr>
<th>Time</th>
<th>Event</th>
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<tr>
<td>7:00 AM</td>
<td>Continental Breakfast</td>
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<td>8:00</td>
<td>Clinical Problem-Solving Exercise</td>
<td>Gurpreet Dhaliwal, MD</td>
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<tr>
<td>9:00</td>
<td>Covid-19: Update on Vaccines and Variants</td>
<td>Monica Gandhi, MD, MPH</td>
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<td>9:55</td>
<td>Break</td>
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<tr>
<td>10:20</td>
<td>The State of the Covid-19 Pandemic</td>
<td>George Rutherford, MD</td>
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<tr>
<td>11:15</td>
<td>Advances in Interventional Endoscopy</td>
<td>Craig Munroe, MD</td>
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<td>12:10 PM</td>
<td>Lunch Break</td>
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<td>12:40</td>
<td>Small Group Workshops: Session II</td>
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<td>8.</td>
<td>The Neurological Exam (repeat)</td>
<td>Vanja Douglas, MD</td>
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<td>9.</td>
<td>Radiology Refresher: Chest Imaging</td>
<td>Brett M. Elicker, MD</td>
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<td>10.</td>
<td>Fundamentals of Preoperative Evaluation</td>
<td>H. Quinny Cheng, MD</td>
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<td>11.</td>
<td>Interesting Cases in Hospital Rheumatology</td>
<td>Sarah Goglin, MD</td>
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<td>12.</td>
<td>Bedside Ultrasound for Diagnosis</td>
<td>Trevor Jensen, MD, MS</td>
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<td>13.</td>
<td>The Art of Diagnostic Reasoning: An Interactive Case</td>
<td>Gurpreet Dhaliwal, MD</td>
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<td>2:00</td>
<td>Session Break- Transition to Next Workshop</td>
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<td>2:10</td>
<td>Small Group Workshops: Session III</td>
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<td>The Neurological Exam (repeat #2)</td>
<td>Vanja Douglas, MD</td>
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<td>15.</td>
<td>Radiology Refresher: Chest Imaging (repeat)</td>
<td>Brett M. Elicker, MD</td>
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<td>16.</td>
<td>Thromboembolism Q&amp;A: Cases and Controversies (repeat)</td>
<td>Tracy Minichiello, MD</td>
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<td>17.</td>
<td>Tough Cases in Medical Consultation</td>
<td>Erika Price, MD, MPH</td>
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<td>18.</td>
<td>Bedside Ultrasound for Diagnosis (repeat)</td>
<td>H. Quinny Cheng, MD</td>
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<td>19.</td>
<td>Management of COVID-19 Patients in the ICU</td>
<td>Trevor Jensen, MD, MS</td>
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<td>20.</td>
<td>Diagnosis and Management of Acute Kidney Injury</td>
<td>Lowell Lo, MD</td>
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<td>3:30</td>
<td>Break</td>
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<td>3:50</td>
<td>Current Controversies in Medical Consultation</td>
<td>H. Quinny Cheng, MD</td>
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<td>4:40</td>
<td>Cardiology Pearls for the Hospitalist</td>
<td>Krishan Soni, MD</td>
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<td>5:30 PM</td>
<td>Adjourn</td>
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<td>Bradley Monash, MD</td>
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P = Pain Credit  
G = Geriatric Credit  
Rx = Meets Requirements for Pharmacotherapeutics CEUs for NPs/Nurses
Diagnosis and Management of VTE in the Hospitalized Patient

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Conflicts of Interest

- I have no actual or potential conflicts of interest in relation to this program or presentation to disclose.

AC FORUM Literature Updates & Rapid Resources

https://acforum-excellence.org/
Objectives

- Splanchnic vein thrombosis
- Calf vein thrombosis
- Outpatient management of PE
- DOACs for VTE in obesity
- Management of anticoagulation in recurrent VTE

A 62 year old man with cirrhosis and history of alcohol use presents with abdominal pain. On exam vitals are stable but abdomen is tender in right upper quadrant. Labs are significant for PLT count of 105K, creatinine 0.8, AST/ALT: 60/30 normal bili, INR 1.0. ultrasound of RUQ shows thrombosis in left and right portal veins. What anticoagulation regimen do you recommend?

1) None—We always see portal vein thrombosis in cirrhosis
2) DOAC
3) LMWH
4) LMWH → warfarin
5) I really don’t like any of these options

Anticoagulation for splanchnic thrombosis

Di Nisio et al. JTN 2020 https://doi.org/10.1111/jth.14836

Splanchnic Vein Thrombosis

Splanchnic Vein Thrombosis Management

Consult surgery if shock, peritonitis, bowel ischemia, GIB

WHO TO TREAT?

- Acute SVT
  - Goal is to prevent bowel ischemia and portal HTN
  - Consider GI eval prior to anticoagulation—particularly in chronic PVT due to varices, portal HTN GIB risk

- Chronic SVT
  - Goal is to prevent progression
  - Risk benefit less clear

Splanchnic Vein Thrombosis-Anticoagulation

HOW TO TREAT?

- Non cirrhotic SVT → DOAC
- Cancer associated symptomatic SVT → LMWH or DOAC
  - Favor LMWH if high bleed risk
- Cirrhotic → LMWH and then switch to DOAC or warfarin if able
- Above assumes not high bleed risk. If high bleed risk multidisciplinary discussion. Consider delay, low intensity AC, withholding

Di Nisio et al. JTN 2020 https://doi.org/10.1111/jth.14836

Case

A 62 year old man with cirrhosis and history of alcohol use presents with abdominal pain. On exam vitals are stable but abdomen is tender in right upper quadrant. Labs are significant for PLT count of 105K, creatinine 0.8, AST/ALT: 60/30 normal bili, INR 1.0. Ultrasound of RUQ shows thrombosis in left and right portal veins. What anticoagulation regimen do you recommend?

1) None—we always see portal vein thrombosis in cirrhosis
2) DOAC
3) LMWH
4) LMWH → warfarin
5) I really don't like any of these options
A 79-year-old man is diagnosed with a **posterior tibial vein DVT**. He is started on therapeutic anticoagulation but a week later he returns to ED with **upper gastrointestinal bleed**. EGD shows gastric ulcer. **Should anticoagulation be resumed on discharge?**

1) Yes, he had a DVT one week ago  
2) No, let’s just get a follow up ultrasound  
3) I like these options even less than the last case

---

**Calf Vein DVT**

- Calf trifurcation DVT (the popliteal vein distal to the knee crease, where it divides into the anterior tibial, posterior tibial and peroneal veins) like proximal DVTs, have annual recurrence risk of 4.7%
- Muscular DVTs (e.g. in the gastrocnemius and soleus veins) have a similar risk of recurrence to deep calf DVT (1.7% vs. 1.6% annual recurrence)
- Proximal DVTs tend to recur more commonly as proximal DVTs and distal DVTs tend to recur more commonly as IDDVT
**Case**

A 79-year-old man is diagnosed with a **posterior tibial vein DVT**. He is started on therapeutic anticoagulation but a week later he returns to ED with **upper gastrointestinal bleed**. EGD shows gastric ulcer. **Should anticoagulation be resumed on discharge?**

1) Yes, he had a DVT one week ago
2) No, let's just get a follow up ultrasound
3) I like these options even less than the last case

---

A 65 year old man with HTN, **weight 130 kg**, presents with pleuritic chest pain. He is hemodynamically stable, O2 sat 95% on RA. CTPE shows segmental PE in RLL. Trop & BNP neg. PESI-O Hestia score **NEGATIVE**. **Should this patient be admitted?**

1) Yes, he has a PE
2) No, looks like he can head home
More than a third of PE patients were treated at home using either the Hestia rule or the sPESI, with a low 30-day rate of complications. All had timely follow-up/clear instructions for discharged patients. This may have contributed to the low rate of complications.

Case
A 65 year old man with HTN, weight 130 kg, presents with pleuritic chest pain. He is hemodynamically stable, O2 sat 95% on RA. CTPE shows segmental PE in RLL. Trop & BNP neg. PESI=0 Hestia score NEGATIVE. Should this patient be admitted?

“In patients with low risk PE we recommend outpatient treatment over hospitalization provided access to medication, ability to access outpatient care, and home circumstance are adequate (strong recommendation).”
A 65 year old man with HTN, weight 130 kg, presents with pleuritic chest pain. He is hemodynamically stable, O2 sat 95% on RA. CTPE shows segmental PE in RLL. Trop & BNP neg. PESI=O Hestia score NEGATIVE. He will be sent home with close follow up with AC clinic and his PCP. What anticoagulation regimen do you recommend?

1) LMWH → warfarin
2) Rivaroxaban
3) Apixaban
4) IV heparin → DOAC
5) Any of the above would work for me

DOACS in VTE & OBESITY

Use of direct oral anticoagulants in patients with obesity for treatment and prevention of venous thromboembolism: Updated communication from the ISTH SSC Subcommittee on Control of Anticoagulation

- DOAC levels not recommended
- Avoid dabigatran/edoxaban due to
- Use LMWH for 1st 4 weeks after bariatric surgery

DOACS in BARIATRIC SURGERY

Martin et al J Thromb Haemost 2021
A 65 year old man with HTN, weight 130 kg, presents with pleuritic chest pain. He is hemodynamically stable, O2 sat 95% on RA. CTPE shows segmental PE in RLL. Trop & BNP neg. PESI=O Hestia score NEGATIVE. He will be sent home with close follow up with AC clinic and his PCP. **What anticoagulation regimen do you recommend?**

1) LMWH→warfarin
2) Rivaroxaban
3) Apixaban
4) IV heparin→DOAC
5) Any of the above would work for me

51 yo man with *diffuse b cell lymphoma* undergoing chemotherapy presents with LUE swelling. He has **PICC line** on that side. U/S shows DVT in brachial→subclavian vein. He is started on enoxaparin 1mg/kg BID. One week later he returns with increased LUE swelling and dilated venous pattern over shoulder and chest and pleuritic chest pain. CT shows **thrombosis up to brachiocephlic vein and 2 subsegmental pulmonary emboli.** **What do you recommend?**

1) Pull PICC and continue dalteparin at current dose
2) Pull PICC and increase dalteparin dose
3) Pull PICC and switch to rivaroxaban

---

**VTE Recurrence on Anticoagulation**

1. **1st-is it REAL?**
   - D-dimer
   - 1 in 3 may have cancer
   - MPO-JAK 2
   - Other exon mutations
   - APLS-beware the INR
   - PNH-hemolysis cytopenias and clots in weird places
   - DOAC-acute VTE vs AFIB

2. **No dose reduction for renal insufficiency with DOAC except edoxaparin**
3. **Warfarin overlap**
Case

51 year old man with *diffuse b cell lymphoma* undergoing chemotherapy presents with left upper extremity swelling. He has **PICC line** on that side. u/s shows **DVT in brachial→subclavian vein**. He is started on dalteparin 200 IU/kg/day. One week later he returns with increased LUE swelling and dilated venous pattern over shoulder and chest as well as pleuritic chest pain. CT shows **thrombosis up to brachiocephalic vein** but not into SVC as well as a sub segmental pulmonary emboli. **What do you recommend?**

1. Pull PICC and continue dalteparin at current dose
2. Pull PICC and increase dalteparin dose
3. Pull PICC and switch to rivaroxaban

Case

65 year old man with **lung cancer** undergoing chemo presents with sudden onset chest pain and SOB. BP 130/80 HR 115, O2 sat 80%. He is found to have **bilateral lobar PE**. Trop and BNP are negative. U/S shows **DVT in right proximal femoral vein**. **What anticoagulant regimen do you start him on?**

1. DOAC-anyone will do
2. LMWH-this is 1st line in cancer associated thrombosis
3. IV heparin, I am thinking about thrombolysis
4. Are we done yet?
Case

65 year old man with **lung cancer** undergoing chemo presents with sudden onset chest pain and SOB. BP 130/80 HR 115, O2 sat 89%. He is found to have **bilateral lobar PE**. Trop and BNP are negative. U/S shows **DVT in right proximal femoral vein**. What anticoagulant regimen do you start him on?

1) DOAC—any one will do
2) LMWH—this is 1st line in cancer associated thrombosis
3) Are we done yet?
Case

65 year old man with lung cancer undergoing chemo presents with sudden onset chest pain and SOB. BP 130/80 HR 115, O2 sat 91%. He is found to have bilateral lobar PE. Trop and BNP are negative. U/S shows DVT in right proximal femoral vein. **What anticoagulant regimen do you start him on if his PLT count is 50K?**

Objectives

- **Splanchnic vein thrombosis**
  - Timing dictates IF anticoag considered; explore etiology; DOACs reasonable in select patients
- **Calf vein thrombosis**
  - Low risk outpatient options include serial u/s, lower intensity, shorter period of time; For most hospitalized patients anticoagulation will be considered BUT know that serial u/s is option in very high bleeding risk patient, or perhaps lower intensity dosing
- **Outpatient management of PE**
  - DOACs for VTE in obesity
    - Reasonable to use but when approaching BMI 50 we are in completely data free zone; always explore history of GI surgery/bariatric surgery; avoid use of DOACs first month post op at least and if used beyond that check trough level
- **Management of anticoagulation in recurrent VTE**
  - Make sure it is real; IF so ask why (patient factors, disease factors), situation dictates anticoagulation choice, maybe switching to DOAC, may be switching oral agents, maybe starting LMWH. THINK CANCER
Questions?

Tracy Minichiello, MD
Update on Clinical Manifestations and Inpatient Management of COVID-19

Management of the Hospitalized Patient
October 21, 2021

Jennifer Babik, MD, PhD
Associate Clinical Professor
Division of Infectious Diseases
University of California, San Francisco

Disclosures

- I have no disclosures.

Learning Objectives

At the end of this lecture, you will be able to:

1. Recognize the diverse clinical manifestations of COVID
2. Identify the indications for COVID-specific and general diagnostic tests in patients admitted with COVID
3. Describe the evidence-based treatments for COVID

Outline

- Clinical Manifestations
- Diagnostics
- Treatment
Outline

- Clinical Manifestations
- Diagnostics
- Treatment

Case #1

31 y/o man with no PMH admitted with fever, sore throat, conjunctival injection, N/V, and chest pain. Found to have elevated troponin (4.55), EF 25%, with course c/b cardiac arrest. Cardiac cath was negative. Chest CTA was negative. CRP was 327.

COVID PCR: initial test negative but repeat positive (Ct value 34)
COVD Ab: nucleocapsid Ab positive

His Troponin Leak is Most Likely:

A. Cardiac injury from demand ischemia
B. Viral myocarditis
C. Pulmonary embolism
D. MIS-A

Case Continued

He was thought to have fulminant myocarditis, possibly due to MIS-A given it seemed COVID infection may have been several weeks prior. He was treated with methylprednisone and IVIG. His cardiac function improved.
Almost Every Organ System Can Be Affected

Neurologic: AMS, delirium, HA, stroke (rare), GBS (rare), encephalitis (rare)
Ocular: conjunctivitis (rare)
ENT: taste and/or smell disorders
Respiratory: cough, dyspnea, URI symptoms
Cardiac: arrhythmias, cardiac injury, myocarditis (rare)
Gastrointestinal: N/V, diarrhea
Renal: acute kidney injury, rhabdo (rare)
Hematologic: DVT/PE (?more common than other respiratory viruses)
Dermatologic: rash (erythematous, urticarial, vesicular), COVID toes

Systemic: Fever, myalgias, fatigue, MIS-A (rare)

Clinical Course

Incubation Period
• Day 0
Symptom Onset
• Day 3
First week of illness
• Day 4
• Fevers, cough, myalgias, loss of taste/smell, diarrhea
• Day 6
Second week of illness
• Day 7
• Dyspnea
• Risk for clinical decompensation, ICU admission, intubation
• Day 14
Persistent Symptoms (Long COVID)
• Day 60
• Fatigue, SOB, sleep d/o

Clinical Manifestations

Day 0
• Fevers, cough, myalgias, loss of taste/smell, diarrhea

Day 3
• Dyspnea
• Risk for clinical decompensation, ICU admission, intubation

Day 6
• Fatigue, SOB, sleep d/o

Multisystem Inflammatory Syndrome in Adults

Systematic review of 221 adults w/ MIS-A

Demographics:
• Median age 21, 70% M, 30% Latina, 36% Black
• 58% no underlying comorbidity

Clinical
• 68% prior (recovered) symptomatic COVID
• Time from symptom onset to MIS-A = 28 day
• Systemic/Cardiac: fever 96%, hypotension 60%, cardiac dysfunction 54%, myocarditis 30%, SOB 52%
• Ocular: Diarrhea 52%, vomiting 44%, conjunctival injection 26%, mucocutaneous lesions 16%

Diagnostics
• Elevated CRP in 90%
• (+) COVID Ab 40%, PCR 25%, both 32%

Treatment
• Steroids 74%, IVIG 55%, other immunomodulators 21%
• 7% died

Think you have a case?
• CDC criteria for MIS-A:
  https://www.cdc.gov/mis/mis-a/hcp.html
• NIH Rx guidelines for MIS-C:
  IVIG/steroids first line, IL-1 antagonist if refractory
• Consult ID, peds ID, rheum, cards

Outline

• Clinical Manifestations
• Diagnostics
• Treatment
### Case #1 Revisited

31 y/o M with no PMH admitted with fever, sore throat, conjunctivitis, N/V, and chest pain. Found to have elevated troponin (4.55), EF 25%, with course c/b cardiac arrest. Cardiac cath was negative. Chest CTA was negative.

COVID PCR: initial test negative but repeat positive (Ct value 34)
COVID Ab: nucleocapsid Ab positive

### What Does a High Cycle Threshold Value Mean?

1. High Viral Load
2. Low Viral Load
3. Does Not Correlate with Viral Load

### Nucleocapsid Antibody Should Be Positive in:

1. Prior Natural Infection
2. Prior Vaccination
3. Both

### Molecular Testing Algorithm in IDSA Guidelines

![Molecular Testing Algorithm Diagram]
Molecular Testing: Highlights of IDSA Guidelines

- Avoid use of OP swab alone
- Patient collected samples acceptable unless NP swab
- Obtain an upper tract sample first → if negative and high suspicion, collect a lower tract sample
- Obtain repeat testing if initial test is negative only in patients where there is high suspicion

Hanson et al, IDSA Guidelines on the Diagnosis of COVID-19: Molecular Testing, 12/2020

Primer on Cycle Threshold (Ct) Values

- Ct value in PCR = number of amplification cycles required to amplify the target gene past a threshold level
- In general, high Ct value = low viral load = less likely to be infectious = longer time from symptom onset
- Beware: sampling technique can affect Ct value

Singanayagam et al, Euro Surveillance 2020

Serology: Timing of the Ab Response In Infection

- Abs become detectable in most patients >14d after symptom onset
- IDSA recommends against using Abs to diagnose COVID in first 2 weeks given risk of false (-)
- Note that IgM and IgG rise at the same time

Key point: Serology may have an adjunct role in diagnosis when suspicion is high and molecular tests are negative - optimal timing is 3-4 weeks after infection


Serology Test Indications

1. To evaluate for COVID in patients where there is high suspicion but molecular testing is repeatedly negative (optimal timing 3-4 weeks after onset)
2. For assessment of MIS-C or MIS-A
3. Epidemiologic surveillance
4. To assess for vaccination response?

Nucleocapsid vs Spike Antibodies

**Natural infection**
- Anti-nucleocapsid
- Anti-spike

**Vaccine induced antibodies**
- Anti-spike

---

**Case #2**

65 y/o woman with asthma presents with 1 week of shortness of breath and is found to be hypoxic requiring 4L. She is COVID positive and admitted. What diagnostic testing does she need?

What diagnostic testing does she need?

A. Basic labs only (CBC, BMP, LFTs, coags)
B. Basic labs and CRP
C. Basic labs and CRP, D-dimer, ferritin, fibrinogen
D. #3 and trend q72 hours

---

**What Labs to Order in a COVID (+) Inpatient?**

- **Initial Labs:**
  - All patients: CBC with diff, BMP, LFTs, coags
  - Consider: procalcitonin, troponin, BNP, lactate
  - Consider to estimate risk for severe disease: D-dimer, CRP, LDH, CK

- **Monitoring**
  - CBC with diff and BMP per usual practice
  - Trent LFTs at least q48h if abnormal at baseline or on remdesivir

---
Other Microbiology Testing

- Respiratory viral testing?
  - Send during flu season (declared by infection control/hospital leadership based on Bay Area flu incidence – currently NOT in flu season)
  - Note, most studies show <0.5% viral coinfection at presentation

- Blood cultures and sputum culture?
  - If considering bacterial coinfection or starting antibiotics
  - Note, most studies show <1.3% bacterial coinfection at presentation
  - Secondary infections can occur (VAP, bloodstream infections, Aspergillus)
  - Send an HIV test if no recent testing

Imaging

- All patients should have a baseline CXR
- Chest CT not needed routinely but consider if there is concern for an additional process (e.g., PE, superimposed bacterial/fungal infection)

Outline

- Clinical Manifestations
- Diagnostics
- Treatment

Treatment Resources

**UCSF Health Internal Guidelines:**
https://infectioncontrol.ucsfmedicalcenter.org/coronavirus/clinical-guidance

**NIH Guidelines on Therapeutic Management of Adults with COVID**

IDSA Guidelines on Treatment of Patients with COVID
**Clinical Course**

- **Incubation Period**
  - Day 0
  - Symptom Onset
  - First week of illness
    - Fevers, cough, myalgias, loss of taste/smell
    - Diarrhea
  - Second week of illness
    - Dyspnea
    - Risk for clinical decompensation, ICU admission, intubation

- **Persistent Symptoms (Long COVID)**
  - Day 5–14
  - Fatigue, SOB, sleep d/o

- **Day 60**
  - Clinical Course
    - Viral Phase → Antiviral Therapies
    - Immune Phase → Immunomodulators
    - Persistent Symptoms (Long COVID)
      - Fatigue, SOB, sleep d/o

**Treatment Overview in Hospitalized Patients**

- **Antivirals**
  - Remdesivir

- **Immunomodulators**
  - Steroids
  - Tocilizumab or Baricitinib

- **Antibodies**
  - Convalescent plasma
  - Monoclonal Antibodies

**Treatment By Clinical Status**

- Inpatient, no O2
- Inpatient, requires O2 by nasal cannula
- Inpatient, requires O2 by HFNC or NIMV
- Inpatient, requires MV or ECMO
Case #3

39 y/o F with no PMH admitted with COVID pneumonia, requiring 2L O2.

She had been taking high doses of acetaminophen and is found to have AST 1250, ALT 1070. She also has AKI with a Cr of 3.5 (normal baseline).

Would You Give Her Remdesivir?

A. Yes
B. No, she is not on enough O2
C. No, because of her LFTs
D. No, because of her AKI

ACTT-1: Most RDV Benefit if only Supplemental O2?

- RCT of 1062 patients w/severe COVID (SaO2<94%, CXR infiltrates, or on O2)
- RDV vs placebo x 10d
- Shortened recovery time from 15 to 10d (p<0.001)
- Benefit greatest if on supplemental O2 only - ? h/c this was largest group (confidence intervals wide in smaller groups) or h/c intubated patients require longer f/u

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Clinical Benefit</th>
<th>Mortality Benefit</th>
<th>NIH Guidelines</th>
<th>UCSF Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient, no O2</td>
<td>May have modest benefit</td>
<td>None</td>
<td>Insufficient data to recommend for or against</td>
<td>Use in patients at high risk for progression or with radiographic e/o LRTI</td>
</tr>
<tr>
<td>Inpatient, requires O2 by nasal cannula</td>
<td>Time to recovery</td>
<td>Possible mortality benefit</td>
<td>Recommended use</td>
<td>Give remdesivir</td>
</tr>
<tr>
<td>Inpatient, requires O2 by HFNC or NIMV</td>
<td>No clear benefit</td>
<td>None</td>
<td>Recommended only with de (not monotherapy)</td>
<td>Give remdesivir</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>No clear benefit</td>
<td>None</td>
<td>Recommended against use</td>
<td>Give remdesivir</td>
</tr>
</tbody>
</table>

Remdesivir: How to Use

Administration:
- 200mg IV x 1 then 100mg IV q24h for 4 additional days
- Do not need to stay inpatient to finish if otherwise ready for discharge
- May consider 10d course if not improving at 5d (usually HFNC, ICU)
- Watch for elevated ALT/AST (discontinue if > 5-10 times ULN)

Renal failure?
- Cyclodextrin vehicle can accumulate in renal failure but likely safe for short course
- Consider risk/benefit if CrCl<30 or HD/CRRT, but usually benefit > risk
- Dose adjustment not needed

Treatment Overview in Hospitalized Patients

Antivirals
- Remdesivir

Immunomodulators
- Steroids
- Tocilizumab
- Baricitinib

Antibodies
- Convalescent plasma
- Monoclonal Antibodies

Case #4
92 y/o M with CAD, DM, dementia is admitted with COVID. He is sitting 94% on 2L. Blood sugars are in the 300s. He is started on remdesivir.

Would You Start Dexamethasone?
A. Yes
B. No
Case Follow-Up

Steroids were initially held given he was on 2L and hyperglycemia, risk of delirium.

He then worsened to required 4L and steroids were started. Blood sugars went into the 400s-500s and steroids were held.

He recovered well and was eventually discharged.

RECOVERY: Dexamethasone by Level of O2

Dexamethasone: Pooled Analysis/Guidelines

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Mortality Benefit</th>
<th>NIH Guidelines</th>
<th>UCSF Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient, no O2</td>
<td>Trend towards harm</td>
<td>Recommend against</td>
<td>Do not give</td>
</tr>
<tr>
<td>Inpatient, requires O2 by nasal cannula</td>
<td>Mortality by 2.7% if on supplemental O2 (7 level with most benefit)</td>
<td>Recommend use when patients require increasing amounts of O2</td>
<td>Give dex when requiring 3-4L O2</td>
</tr>
<tr>
<td>Inpatient, requires O2 by HNMD or NIMV</td>
<td>Mortality by 2.7% if on supplemental O2 (7 level with most benefit)</td>
<td>Recommend use</td>
<td>Give dex</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>Mortality by 34%</td>
<td>Recommend use</td>
<td>Give dex</td>
</tr>
</tbody>
</table>

Dexamethasone: How to Use

- 6mg IV/PO x 10d or until hospital discharge, whichever comes first (PO preferred)
- If dexamethasone is unavailable, equivalent doses of other glucocorticoids may be used
- Factors to consider if you might withhold or stop steroids:
  - Uncontrolled invasive fungal infection
  - Uncontrolled hyperglycemia
  - Existing delirium
  - Active GI bleeding
Case #5

71 y/o M with melanoma (not on chemo) admitted with COVID 2 days ago. On admission he was requiring 2-3L but has had rapid worsening since admission and is just now transferred to the ICU requiring 30L HFNC.

What Treatments Would You Give?

A. Remdesivir, dexamethasone
B. Remdesivir, dexamethasone, baricitinib
C. Remdesivir, dexamethasone, tocilizumab
D. Remdesivir, dexamethasone, baricitinib, tocilizumab

Tocilizumab (Anti-IL6R)

- Multiple smaller RCTs showed no mortality benefit
- The 2 largest RCTs (REMAP-CAP and RECOVERY) did show a mortality benefit
- May be due to differences in patient population or baseline steroid use
  - Benefit seen in sicker patients early in course with associated inflammatory response
  - Benefit seen in studies with high background steroid use

Tocilizumab: RCTs with Mortality Benefit

<table>
<thead>
<tr>
<th>RCT</th>
<th>Inclusion Criteria</th>
<th>Characteristics</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECOVERY</td>
<td>Sats&lt;92% RA or on O2 and CRP ≥ 75 mg/L</td>
<td>82% steroids</td>
<td>Lower mortality - 29% tocil vs 33% SOC (OR 0.86, CI 0.77-0.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median duration of hospitalization: 2 days</td>
<td>Shorter time to d/c in tocil group</td>
</tr>
<tr>
<td></td>
<td></td>
<td>41% HFNC/NIV/TV, 14% MV</td>
<td>3 serious bacterial infections thought due to tocil</td>
</tr>
<tr>
<td>REMAP-CAP</td>
<td>Admitted to ICU within 24 hrs</td>
<td>90% steroids</td>
<td>Lower mortality - 28% tocil vs 36% SOC (OR 1.64, CI 1.14-2.35)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median duration of hospitalization: 1.2d</td>
<td>Shorter duration of organ support</td>
</tr>
<tr>
<td></td>
<td></td>
<td>71% HFNC/NIV/TV, 29% MV</td>
<td>1 secondary bacterial infection in tocil group</td>
</tr>
</tbody>
</table>

Baricitinib (JAK inhibitor): RCT Data

<table>
<thead>
<tr>
<th>Trial Design</th>
<th>Characteristics (note lack of data for MV)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTT-2</td>
<td>RDV + baricitinib + tocilizumab vs RDV + placebo</td>
<td>• Only 12% got steroids</td>
</tr>
<tr>
<td></td>
<td>(n=1033)</td>
<td>• 14% RA, 55% supp-O2, 21% HfN/O2, 13% MV</td>
</tr>
<tr>
<td>COVID BARRIER</td>
<td>Baricitinib + CRP 2x CRP, ferritin, D-dimer</td>
<td>75% got steroids</td>
</tr>
<tr>
<td>(n=1153)</td>
<td></td>
<td>12% RA, 64% supp-O2, 24% HfN/O2, 13% MV</td>
</tr>
<tr>
<td>STOP COVID</td>
<td>Tocilizumab vs placebo hospitalized &lt;3d</td>
<td>85% got steroids</td>
</tr>
<tr>
<td>(n=249)</td>
<td></td>
<td>25% RA, 83% supp-O2, 13% HfN/O2</td>
</tr>
</tbody>
</table>

Tocilizumab and Baricitinib: Guidelines

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<thead>
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<td><em>+</em></td>
<td>Do not give</td>
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<tr>
<td>Inpatient, requires O2 by nasal cannula</td>
<td>Insufficient evidence to clearly characterize subgroups who would benefit</td>
<td>Do not give</td>
</tr>
<tr>
<td>Inpatient, requires O2 by HfN or IMV</td>
<td>Recommend baricitinib or tocilizumab if recently hospitalized (&lt;7d), rapidly increased O2, systemic inflammation</td>
<td>Baricitinib if recent hospitalization (&lt;5 d) and rapidly worsening</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>Recommend tocilizumab if within 24 h of admission to ICU</td>
<td>Tocilizumab if hospitalized &lt;5d and in ICU O2 and rapidly progressing ICU or requiring MV</td>
</tr>
</tbody>
</table>

Tocilizumab and Baricitinib: Notes

- Give one or the other, NOT both
- They should be given in combination with steroids
- If there are drug shortages, per NIH Guidelines can substitute tofacitinib (for baricitinib) or sarilumab (for tocilizumab)
- Consider screening for (or empirically treating for) Strongyloides before starting tocilizumab
- Use with caution in immunocompromised patients (but we still usually give)
- Relatively contraindicated if a patient has a concomitant serious infection

How to Give

**Tocilizumab**
- Tocilizumab 8mg/kg IV x 1 (based on actual body weight, max dose 800mg)
- Contraindicated if ANC < 500, platelets < 50, ALT > 5x ULN

**Baricitinib**
- Baricitinib 4mg PO daily x 14d or until hospital d/l (whichever comes first)
- Renally dose if CrCl<60, contraindicated if CrCl<35
- Need to discontinue if ANC<200, ANC<500, or AST/ALT >10x ULN
Case #5: continued

Given ICU team’s suspicion he would be intubated that evening, we gave tocilizumab x 1.

He was not actually intubated until several days later. He had a prolonged ICU stay with multiple complications and was eventually transitioned to comfort care.

Convalescent Plasma

**Data:**
- Multiple RCTs, pooled analysis of 11 RCTs → no mortality benefit
- One exception: Libster et al showed ↓-risk progression if early, mild disease, high risk patient

**Guidelines**
- NIH: Recommends against
- UCSF: <72h symptom onset + non-severe disease (~RA) + high risk for progression (criteria from Libster et al, rare to meet these in practice)

Convalescent Plasma in Immunocompromised?

**Data**
- Little comparative data although in REMAP-CAP there was possible benefit (↑-organ support free days) in the subgroup of immunosuppressed patients (but only 6% of the trial)

**Guidelines**
- NIH: insufficient data to recommend for or against
- UCSF: consider in patients with severe immunocompromise + not expected to mount Ab response
Monoclonal Abs in Hospitalized Patients

- ACTIV-3 ➔ no benefit of bamlanivimab in hospitalized patients
- Guidelines in hospitalized patients:
  - NIH: Monoclonal Abs not authorized for hospitalized patients unless patient is hospitalized for another reason and happens to have mild-moderate COVID (e.g., admitted for hip fracture but then found to have mild-moderate COVID)
- Recovery Trial (still in preprint):
  - Casirivimab/imdevimab combination reduced risk of death by 20% in hospitalized patients who were seronegative (24% vs 30%, RR 0.8, p<0.001)
  - Also led to shorter LOS and lower risk progression to MV/death
  - Stay tuned but not currently authorized for use in hospitalized patients

Summary: NIH Treatment Guidelines

- Inpatient, no O2
  - Remdesivir
  - Dexamethasone
  - No baricitinib or tocilizumab

- Inpatient, requires O2 by nasal cannula
  - Remdesivir
  - Dexamethasone
  - Baricitinib if recent hospitalization (eg 3-4d) + rapidly worsening

- Inpatient, requires O2 by HFNC or NIMV
  - Remdesivir
  - Dexamethasone
  - Tocilizumab if hosp <3h and ICU <24h and rapidly progressing to MV or requiring MV

- Inpatient, requires MV or ECMO
  - Remdesivir
  - Dexamethasone
  - Tocilizumab if hosp <3h and ICU <24h and rapidly progressing to MV or requiring MV

Molnupiravir

- Studied in outpatients with mild-moderate COVID with symptom onset <5 days ➔ reduced risk of hospitalization or death by 50%
  (press release)
- EUA application filed with FDA ➔ stay tuned

Summary: UCSF Treatment Guidelines

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>UCSF Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient, no O2</td>
<td>Remdesivir, Dexamethasone, No baricitinib or tocilizumab</td>
</tr>
<tr>
<td>Inpatient, requires O2 by nasal cannula</td>
<td>Remdesivir, Dexamethasone</td>
</tr>
<tr>
<td>Inpatient, requires O2 by HFNC or NIMV</td>
<td>Remdesivir, Dexamethasone</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>Remdesivir, Dexamethasone</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>Remdesivir, Dexamethasone</td>
</tr>
<tr>
<td>Inpatient, requires MV or ECMO</td>
<td>Remdesivir, Dexamethasone</td>
</tr>
</tbody>
</table>

Mjolnir

Molnupiravir press release, October 1, 2021.
**Antibiotics**

- Bacterial coinfection on admission to the hospital is very uncommon (<1-3% across multiple studies)
- Most patients do not need to be covered for CAP

**Anticoagulation**

- Prophylactic anticoagulation should be given unless contraindicated
- Therapeutic anticoagulation
  - Critically ill: No benefit, ↑ major bleeding – do not use
  - Noncritically ill:
    - REMAP-CAP, ACTIV-4, ATTACC (n=2231): ↑ survival without organ support (79% vs 75%); no difference survival; ↑ major bleeding (1.9% vs 0.9%)
    - HEP-COVID (n=253): ↓ composite thrombosis/death (but did ax screen for VTE, small study), no difference in major bleeding
    - Jury still out here, could consider in patients with noncritical COVID and no contraindications

**Take Home Points**

- COVID can affect all organ systems
- Most admitted patients just need basic labs
- For most patients, consider if they need remdesivir, dexamethasone, and baricitinib vs tocilizumab
- Most patients do not need antibiotics

**Questions?**

October 2020  
October 2021
MANAGEMENT OF ANTICOAGULATION IN THE HOSPITALIZED PATIENT

Tracy Minichiello, MD
Professor of Medicine
University of California, San Francisco
Chief, Anticoagulation and Thrombosis Services
San Francisco, VA Medical Center

Conflicts of Interest

I have no actual or potential conflicts of interest in relation to this program or presentation to disclose.

Objectives

- Anticoagulation in COVID-19
- ASA + anticoagulation
- Anticoagulation for AFIB in ESRD


A. Prophylactic dose
B. Intermediate dose
C. Therapeutic dose
D. Yes
SARS-CoV2 AND THROMBOSIS
Iba et al. CCMJ July 2020

Clotting of CRRT/ECMO circuits
5.5% to 14.1%
Implicated in disease progression ARDS

Joan Loo et al. Thorax 2021;76:412-420

Ackermann NEJM May 2020

Autopsy studies identified unsuspected VTE in situ pulmonary arterial thrombosis in more than 60% of pts w/COVID-19, suggesting thrombosis contributes to mortality.

↑ D-dimer, especially > 4x ULN predict a more than 2-fold ↑ risk of VTE/mortality
Anticoagulation for Thrombosis Prevention in COVID

- What dose of anticoagulation should be used in critically ill patients hospitalized with COVID
- What dose of anticoagulation should be used in moderately ill patients hospitalized with COVID
- Should patients hospitalized with COVID be discharged on anticoagulation for thrombosis prevention

MULTIPLATFORM TRIALS

**What dose of anticoagulation in the Critically Ill COVID 19**

- Support free: No
- Organ free: Support
- High flow nasal cannula
- Mechanical ventilation
- ECMO
- Noninvasive ventilation
- Invasive ventilation

**What Dose of Anticoagulation in Moderately Ill COVID**

- Trial stopped early
- Organ free support
- High flow cannula
- Noninvasive ventilation
- Invasive ventilation

Regardless of D-dimer

MULTIPLATFORM TRIALS

CRITICALLY ILL PATIENTS

PROPHYLACTIC DOSING OF ANTICOAGULATION

Therapeutic Anticoagulation with Heparin in Critically Ill Patients with COVID-19

NONCRITICALLY ILL PATIENTS

THERAPEUTIC DOSING OF ANTICOAGULATION

ACTION TRIAL – Rivaroxaban in COVID-19

Is therapeutic anticoagulation with rivaroxaban effective in preventing complications in patients hospitalized with COVID (90% moderately ill) & ↑ D-dimer?

In patients hospitalized with COVID-19 with elevated D-dimer levels, initial in-hospital therapeutic anticoagulation with rivaroxaban 20 mg once daily for stable patients or enoxaparin for unstable patients followed by rivaroxaban through 30 days did not improve clinical outcomes and increased bleeding compared with in-hospital prophylactic anticoagulation.

Lopes RD et al. Lancet 2021 https://doi.org/10.1016/S0140-6736(21)01203-4

Therapeutic Anticoagulation in Moderately Ill Covid

Survival to DC
- therapeutic anticoagulation 92.7%
- usual care 91.8%

Progression to intubation/death
- Therapeutic anticoagulation 10.9%
- Usual care 12.1%

Major thrombosis or death
- Therapeutic anticoagulation 8%
- Usual care 9-9%


Therapeutic Anticoagulation for Thromboprophylaxis in COVID 19

Spyropolos AC et al. JAMA Intern Med 2021
Therapeutic Anticoagulation for Thromboprophylaxis in COVID-19

- 257 patient hospitalized with COVID-19
- Supplemental O2 and D-dimer > 4x ULN or SIC score ≥4.
- Primary outcome composite of VTE, ATE, and all-cause mortality within 30 days of hospitalization
- All had U/S at HD 10 + 4 or at discharge if sooner.

<table>
<thead>
<tr>
<th></th>
<th>standard</th>
<th>therapeutic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint (VTE)</td>
<td>41.9% (29%)</td>
<td>28.7% (10.9%)</td>
</tr>
<tr>
<td>ICU</td>
<td>55.3%</td>
<td>51.1%</td>
</tr>
<tr>
<td>Non ICU</td>
<td>36.1%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Death</td>
<td>25%</td>
<td>19.4%</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>2.8%</td>
<td>4.7%</td>
</tr>
</tbody>
</table>

Spyropolos AC et al JAMA Int Med 2021

NON ICU:
NNT 5
NNH 33

POST DISCHARGE PROPHYLAXIS FOR COVID

MICHELLE trial-publication pending

- Evaluate rivaroxaban 10 mg po daily vs control among discharged patients hospitalized for ≥3 days WITHOUT CKD, dual antiplt, surgery/trauma in past month or any bleeding in past 3 months with COVID-19
- IMPROVE score ≥4 OR IMPROVE SCORE > 2-3 PLUS elevated d-dimer (≥500 ng/ml)
- Primary outcome symptomatic VTE, VTE death, ATE, MI., stroke

3.1% rivaroxaban 9.4% control, no major bleeding in either arm

Ramaccioti et al Ann Heart J 2021

Case

62 yo admitted to hospital with COVID-19 requiring 3 L oxygen
Classic chest x-ray and inflammatory markers. Normal kidney and liver function D-dimer elevated at 2000 ng/dL. What dose of anticoagulation prophylaxis do you recommend?

A. Prophylactic dose
B. Intermediate dose
C. Therapeutic dose
D. Yes

MODERATELY ILL PATIENTS – Consider D-dimer, Oxygen status, bleeding risk

PROPHYLACTIC vs. THERAPEUTIC ANTICOAGULATION
A 75 year old man with HFpEF, DM, HTN is admitted with CHF exacerbation and new AFIB. You are going to start him on a DOAC. He is on ASA for primary CAD prevention. Do you continue this in addition to his full dose DOAC?

1) Yes, he has a lot of risk factors for CAD
2) No, I think the DOAC should cover it
3) I am going to defer this to the PCP

**ASA & ANTICOAGULATION**

**MANY INDICATIONS FOR ASA**
- Primary prevention of CAD
- PAD
- Secondary prevention of CAD, CVA, VTE

**SHOULD PATIENTS ON ANTICOAGULATION BE ON ASA TOO?**
Hundreds of thousands of patients in the US are on BOTH ASA plus AC
Commonly agreed upon indications for dual therapy: ACS, recent PCI, CABG
You have this slide on RISK. You really need a slide on BENEFIT of combo therapy - or lack thereof.
Moll, Stephan, 9/16/2021
Case

A 75 year old man with HFpEF, DM, HTN is admitted with CHF exacerbation and new AFIB. You are going to start him on a DOAC. He is on ASA for primary CAD prevention. Do you continue this in addition to his full dose DOAC?

1) Yes, he has a lot of risk factors for CAD
2) No, I think the DOAC should cover it
3) I am going to defer this to the PCP

A 75 year old man with PAD (iliac bypass 18 months ago), HTN DM is admitted with new AFIB with rapid ventricular response. You are going to start him on a DOAC. He is on ASA for his PAD. Do you continue this in addition to his full dose DOAC?

1) Yes, he needs it for PAD
2) No, I think the DOAC should cover it
3) I am going to defer this to the PCP

European Society of Cardiology 2021 Consensus

Peripheral Artery Disease

If peripheral stent short term clopidogrel in addition to AC (~1 month)
Add ASA (triple therapy) ONLY in select cases at highest risk ie, prior stent thrombosis, slow flow

Patients with peripheral arterial disease and concomitant indication for oral anticoagulation

Key messages: Antithrombotic strategies in patients with PAD and other indications requiring anticoagulation.

- When dual-dose OACs are indicated for other conditions in patients with chronic PAD, the addition of aspirin therapy should generally be avoided because of bleeding risk, unless a more proximal endovascular intervention was performed.
- SAPT in addition to OAC may be considered in patients at high distal risk, enrolling the bleeding risk and thrombosis.

For Heart J, download: https://doi.org/10.1093/eurheartj/ehab390
Case

A 75 year old man with PAD (iliac bypass 18 months ago), HTN, DM is admitted with new AFIB with rapid ventricular response. You are going to start him on a DOAC. He is on ASA for his PAD. Do you continue this in addition to his full dose DOAC?

1) Yes, he needs it for PAD
2) No, I think the DOAC should cover it
3) I am going to defer this to the PCP

Case

A 60 year old man with HTN and mechanical aortic valve placed 2017 is on warfarin and ASA. He is admitted for GIB. INR is 2.0 on admission, warfarin is held and he has EGD which shows gastric ulcer which is treated endoscopically. His Hgb stabilizes and he resumes his warfarin. Should he resume his ASA as well?

1) Yes, he needs it for his mechanical valve
2) No, I think the warfarin should cover it
3) I am going to defer this to the PCP

Prior recommendations to add low-dose ASA to therapeutic VKA were based on studies performed decades ago that included older-generation prostheses and additional risk factors:}

CM Otto et al. Circulation 2020
It is decided to resume warfarin therapy but to stop the ASA. Should he be bridged?

1) Yes, he needs it for his mechanical valve
2) No, I think the warfarin monotherapy should cover it
3) I am going to defer this to his PCP

Case

It is decided to resume warfarin therapy but to stop the ASA. Should he be bridged?

1) Yes, he needs it for his mechanical valve
2) No, I think the warfarin monotherapy should cover it
3) I am going to defer this to his PCP

79-year-old female with DM and ESRD is transferred to the ED from her dialysis center for dizziness, shortness of breath. She is 62 kg, normal BP HR, normal aPTT/PT, CBC, thyroid, liver; SCr 6.3 mg/dL. ECG shows AFIB. ECHO without valvular disease. Should she be started on anticoagulation?

1) Yes, would start apixaban
2) Yes, would start warfarin
3) No, I am going to defer this to the PCP
**What About Age?**
Declining benefit:
- Age > 87: warfarin
- Age > 92: apixaban

**Warfarin for AFIB in ESRD**
- Randawa JAMA 2020
- Kuno JACC 2020
- Pokorney 2020

**DOACS for AFIB in ESRD**
- Apixaban FDA approved for use in ESRD for AFIB (not VTE)
- Based on single dose of 5 mg apixaban recommended no dose adjustment—same dosing algorithm as those not on HD. But subsequent studies showed accumulation of drug at this dose, but not at 2.5 mg BID dosing.
**ESRD-specific Risk Assessment?**

- 90% ESRD have CHADS2-vasc≥2
- Not validated in ESRD
- Overestimates stroke risk
- Risk may outweigh benefits

---

**What the AF Guidelines Say**

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Stroke prevention with anticoagulation in ESRD ± dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA/HRS 2019&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• May be reasonable to prescribe warfarin or apixaban (IIb)</td>
</tr>
<tr>
<td>KDIGO 2020&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Primary prevention</td>
</tr>
<tr>
<td></td>
<td>• Decision to anticoagulate and choice of agent should be discussed with nephrologist</td>
</tr>
<tr>
<td></td>
<td>• Refers to ACC/AHA/HRS recommendations</td>
</tr>
<tr>
<td></td>
<td>• Consider left atrial appendage occlusion if additional bleed risks</td>
</tr>
<tr>
<td>CCS/CHRS 2020&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Secondary prevention</td>
</tr>
<tr>
<td></td>
<td>• Suggest patients not routinely receive antithrombotic therapy (Weak recommendation)</td>
</tr>
<tr>
<td></td>
<td>• Individualized on risk vs. benefit and patient preference</td>
</tr>
<tr>
<td>ESC/EACTS 2021&lt;sup&gt;4&lt;/sup&gt;</td>
<td>• Evidence is limited (no specific recommendation)</td>
</tr>
</tbody>
</table>

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1. January et al. 2019. doi: 10.1161/CIR.0000000000000665; Kelly et al. Stroke 2021 https://doi.org/10.1161/STROKEAHA.120.029680
3. CCS/CHRS 2020
4. ESC/EACTS 2021

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*De Vriese et al. Nephrol Dial Transp 2021*

*What the AF Guidelines Say*
CONSIDER ANTICOAGULATION FOR AFIB IN ESRD

IF
- Patient amenable through shared-decision making
- Places higher value on avoiding stroke than bleed
Apixaban is an option for the patient

AND
- Thorough risk/benefit analysis of thrombosis/bleed/frailty is done
- No need for DAPT (recent stent, TAVR)
- Optimization of other parameters to avoid adverse events (BP, etc)

BUT
- If these are not possible, consider LAAO with Watchman or Amulet recognizing patient will require brief period of antithrombotic therapy after placement

1. www.cardiosmart.org/SDMAFib?_ga=2.87317343.67355683.1631903462-1257589260.1631903462

79-year-old female with DM and ESRD is transferred to the ED from her dialysis center for dizziness, shortness of breath and “flip-flopping” sensation in her chest, “similar to episodes over the last month but worse…”

She is 62 kg, normal BP HR, normal aPTT/PT, CBC, thyroid, liver Scr 6.3 mg/dL. ECG shows AFIB. ECHO without valvular disease.

**Should she be started on anticoagulation?**
1) Yes, would start apixaban
2) Yes, would start warfarin
3) No, I am going to defer this to the PCP

Objectives
- Anticoagulation in COVID 19
  - No anticoagulation prior to admission, no compelling evidence for anticoagulation after DC in all patients; all patient admitted with COVID receive at least prophylactic anticoagulation - critically ill PROPHYLAXIS, moderately ill PROPHYLAXIS vs THERAPEUTIC
- ASA + anticoagulation
  - Avoid when possible. Reserve for those in whom benefit outweighs the risk, TALK TO YOUR COLLEAGUES vascular, cardiology, neurology
- Anticoagulation for AFIB in ESRD
  - NO GOOD DATA; warfarin not benign, DOACs maybe alternative but high level data lacking and dosing still unclear

Questions?

Tracy Minichiello, MD
ASA IS A HUGE RISK FACTOR FOR GIB ON AC. 40% of AC-related bleeds on ASA.

We don’t know if PPI provide PRIMARY prevention of GIB cessation.

**RESUMPTION OF AC AFTER GIB**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Mortality of Recurrent event</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFIB</td>
<td>25%</td>
</tr>
<tr>
<td>Secondary prevention VTE</td>
<td>4%</td>
</tr>
<tr>
<td>Secondary prevention VTE in cancer</td>
<td>15%</td>
</tr>
</tbody>
</table>

Review medical, blood, and read. Consider stopping dose. Benefit of ASA outweigh risk?
Case 1

- A 65 year-old right handed man with a history of HTN presented to the ED in a delayed fashion after the sudden onset of right sided weakness.
- Exam shows expressive aphasia, R face and arm weakness as well as R visual field cut and L gaze deviation.
- He was last seen normal at 1 p.m., and it is now 10:45 pm.

What treatment should this patient likely receive?

A. IV t-PA alone
B. IV t-PA followed by embolectomy
C. Embolectomy alone
D. IV heparin
E. Antiplatelets
The 2021 Acute Stroke Timeline

- Time of onset = last time seen normal
- 0-4.5 Hours: IV-tPA
- 0-6 Hours: Mechanical Embolectomy for all
- 6-24 Hours: Mechanical Embolectomy for some

Intravenous t-PA: Broad Success

Intravenous t-PA: Broad Success

Embolectomy in NeuroIR Suite

Pre-treatment

Post-treatment

Speed Matters: Time is Brain

- Examination of the Get With the Guideline Registry in the U.S. over the last decade
  - 1400 hospitals, nearly 59,000 patients
  - Mean time to treatment was 144 minutes
    - Earlier on weekdays, more severe stroke, arrival in ambulance
- For every 15 min earlier administration...
  - Significantly lower in-house mortality
  - Significantly lower rates of ICH
  - Significantly more independent ambulation at d/c
  - Significantly higher rate of d/c to home


The 2015 Endovascular Revolution

- Five major positive trials of endovascular therapy all published in 2015 in NEJM
- Trial design somewhat differed, but common to each:
  - 1. Used newer-generation devices
  - 2. Selected patients who were eligible via CTA
  - 3. IV t-PA in those who were eligible followed by embolectomy
  - 4. Typically a 6 hour time window

The 2018 Second Revolution

- DAWN and DEFUSE3 Trials
- Select patients with LVO treated up to 24 hours based on CT perfusion selection
  - Automated CT software widely available
- Has led to major reexamination of triage and ED/hospital protocols


What do we do given this data?

- 1. All patients eligible for IV t-PA should receive it (quickly)
- 2. Patients within 6 hours should receive a CTA to look for a large vessel occlusion (LVO)
- 3. If LVO present, endovascular therapy should occur, even following IV t-PA regardless of perfusion data

What do we do given this data?

- 4. If the patient has a LVO and presents between 6-24 hours, CT perfusion is required and selects patients who should receive endovascular therapy
- 5. Very late endovascular cases may emerge as still possible with favorable perfusion
What is coming up in acute stroke?

- Teneceplase as an alternative to t-PA
  - Easier to administer with identical outcomes
- Skip the t-PA before embolectomy?
  - Large study failed to show benefit


What is coming up in acute stroke?

- Very late treatment of LVO in patients with favorable perfusion
  - 24 hours was selected for trials on no specific scientific basis

Kim B et al: JAMA Neurol 2020

Case 2

- A 65 year-old man with a history of HTN presents with 3 days of R arm weakness
- Examination shows a R pronator drift and mild weakness in the extensors of the R hand and arm
- The patient takes aspirin 81mg daily as well as HCTZ

Which of the following is not part of the standard embolic stroke workup?

A. Echocardiogram
B. Extended cardiac telemetry
C. Lipid panel
D. B12, TSH, RPR, ESR
E. Carotid evaluation
Standard Large-Vessel Stroke Workup

- Cardioembolic: afib, clot in heart, paradoxical embolus
  - 1. Telemetry
  - 2. TEE with bubble study
- Aortic Arch
  - 2. TEE with bubble study
- Carotids
  - 3. Carotid Imaging (CTA, US, MRA, angio)
- Intracranial Vessels
  - 4. Intracranial Imaging (CTA, MRA, angio)

And evaluate stroke risk factors

TEE vs. TTE

- 231 consecutive TIA and stroke patients of unknown etiology underwent TTE and TEE
- 127 found to have a cardiac cause of emboli, 90 of which (71 percent) only seen on TEE
- TEE superior to TTE for: LA appendage, R to L shunt, examination of aortic arch
- More recently: TEE found additional findings in 52% and changed management in 10%


Atrial Fibrillation Detection

- EKG
- 48 Hours of Telemetry
- Long-term cardiac event monitor (>21d)
  - 15-20% of patients with cryptogenic stroke otherwise unexplained had afib detected
  - Clearly changes management
  - Probably cost effective


Really Long Term Monitoring: 2021

- STROKE-AF: randomized trial comparing usual care with ICM for 1 year
  - 492 patients aged 60 (or 50 with 1 stroke risk factor) who had stroke within 10 days
  - Afib found in 12.1% vs 1.8%
  - Large and small vessel strokes included
  - Clinical significance not certain

Bernstein RA et al: JAMA 325:2169, 2021
Approach to Stroke Treatment

Acute Stroke Therapy?

No

Anticoagulants?

No

Antiplatelets

Shrinking Indications for Anticoagulation in Stroke

1. Atrial Fibrillation
2. Some other cardioembolic sources
   - Thrombus seen in heart
   - ?EF<35
   - ?PFO with associated Atrial Septal Aneurysm
3. Vertebral or Carotid dissection
4. Rare hypercoagulable states: APLS

The “Absolute Mess” of PFO in Stroke

• Around 20-25% of all patients have a PFO
• PFO alone is not necessarily associated with higher risk of recurrent stroke
  - Higher risk: Larger PFO, associated atrial septal aneurysm, perhaps younger age
• Three previous negative trials of closure devices but cardiologists pre-2017 were still performing these procedures widely

More Actionable Data

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>RESPECT</th>
<th>Gore REDUCE</th>
<th>CLOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptogenic stroke within past 270 days + PFO</td>
<td>Cryptogenic stroke within past 180 days + PFO</td>
<td>Stroke attributed to PFO + atrial septal aneurysm OR large PFO</td>
<td></td>
</tr>
<tr>
<td>Participants</td>
<td>960 participants</td>
<td>644 participants</td>
<td>663 participants</td>
</tr>
<tr>
<td>Intervention Arm</td>
<td>PFO closure</td>
<td>PFO closure + antiplatelet</td>
<td>PFO closure + antiplatelet</td>
</tr>
<tr>
<td>Medical Rx Arm</td>
<td>Antiplatelet or anticoagulation</td>
<td>Antiplatelet</td>
<td>Arm 1: antiplatelet Arm 2: anticoagulation</td>
</tr>
<tr>
<td>Results</td>
<td>Less recurrent stroke with PFO closure (NNT 42)</td>
<td>Less recurrent clinical and clinical/radiographic stroke with PFO closure (NNT 28)</td>
<td>Less recurrent stroke with PFO closure (NNT 20)</td>
</tr>
</tbody>
</table>

What now? “Let’s close all these PFOs!”

- DO NOT close all these PFOs
- DO screen patients for PFO (?how)
- It is sensible to discuss with your cardiologists some “Rules of the Road”
- At the end of the day, this is an exciting advance for some (young) people with stroke that can make a substantial impact on recurrence rates

Rules of the Road

- Consider PFO closure if:
  - The patient is younger than 60 years old
  - AND you can be sure the PFO is the most likely etiology after a thorough workup
  - AND the qualifying event is a stroke (not TIA) that appears embolic (not lacunar)
  - Likely concentrate on large PFOs or those with an atrial septal defect
  - Cardiologists new task: start counting bubbles

Heparin in Acute Stroke

- Study examined the largest trials of heparin, heparinoids, LMWH in acute stroke
- Could find no benefit even in those patients with highest risk of recurrent ischemia and lowest risk of hemorrhage
- Considering use of heparin for “selected patients” therefore seems unwise

Case 3

- A 70 year-old woman with a history of DM, smoking presents 10 hours after the onset of slurred speech and right arm and leg weakness.
- The patient is taking ASA 81mg daily
Stroke workup is unrevealing. Your Treatment?

A. Increase ASA to 325mg daily
B. Add Plavix to ASA
C. Stop ASA, start Plavix
D. Stop ASA, start Aggrenox
E. Anticoagulate

### Approach to Stroke Treatment

**Acute Stroke Therapy?**

- No

**Anticoagulants?**

- No

**Antiplatelets**

### Antiplatelet Options

- 1. ASA
  - 50mg to 1.5g equal efficacy long-term
- 2. Aggrenox
  - 25mg ASA/200mg ER Dipyridamole
- 3. Clopidogrel (Plavix)
  - Multiple secondary prevention studies (CHARISMA, SPS3) show no long-term benefit in combination with ASA

### Antiplatelet Options

- If on no antiplatelet medication
  - Plavix vs. Aggrenox (or ASA)
- If already on ASA
  - Switch to Plavix vs. Aggrenox
- If already on Plavix or Aggrenox
  - ???
**Clopidogrel + ASA: Ever A Winning Combination?**

- **POINT trial**
- Select those with only minor or no deficits (NIHSS 3 or less or ABCD2 of 4 or more)
- Nearly 5000 TIA or Minor Stroke patients assigned to 90d of daily ASA + Placebo versus daily ASA + Clopidogrel following 600mg load
- Modestly improved efficacy (1.5%)
- Minimally (0.5%) more hemorrhage

![Graph]

**Ticagrelor: Another Short-term DAPT Option**

- **THALES trial (like POINT trial)**
- Nearly 11000 TIA or Minor Stroke patients assigned to 30d of daily ASA + Placebo versus daily ASA + Ticagrelor following 180mg load
- Modestly improved efficacy (1.1%)
- Severe bleeding in 0.5%
- When to use?

![Graph]

**When to use Dual Antiplatelets**

- NOT all the time!
- After minor stroke or TIA for only 21* days
- After a fresh carotid or coronary stent
- With severe intracranial atherosclerosis (>70%) and stroke/TIA in that territory for only 90 days

**Other Acute Stroke Management**

- Statins for (almost) all patients with stroke or TIA
  - 80mg atorvastatin if LDL>100 for at least 5 years
- Tight Glucose and Fever control in acute period
- Enoxaparin for DVT prophylaxis (better than compression stockings or UFH)
Permissive Hypertension

• National Guidelines
  – To at least 220/120
  – After IV tPA: less than 185 systolic for 24 hours
• We typically stop all meds except half-dose β-blockers and (maybe) clonidine

Permissive Hypertension

• When to stop remains controversial
• Situations where more important
  – Large Vessel Occlusion
  – Fluctuating symptoms
• We begin a medicine before discharge (~72h) and aim for normotension over a matter of weeks
  – Choose thiazides and ACEI first

Case 4

• A 73 year-old woman with HTN comes to the ED after a 5 minute episode of right arm weakness that has since resolved.
• Exam is normal except blood pressure is elevated at 176/97

Other than TIA, what is the most common neurologic diagnosis here?

A. Conversion disorder
B. Migraine
C. Focal Seizure
D. UTI
E. Cervical spine lesion
TIA versus Stroke

- Up to 30-50% of TIA have infarct on MRI
- Conceptually the same disorder
  - Same workup, same treatment
- Pendulum swing
  - Pre-2001: Much more aggressive with stroke
  - 2002-2007: TIA and stroke equally aggressive
  - 2008-present: A more aggressive approach with TIA outside of the acute treatment window

Risk of Future Stroke with TIA: ABCD² Score

- 7-day risk overall 8.6-10.5 percent
- Age
  - >60 =1 point
- Blood Pressure
  - SBP>140 or DBP>90 =1 point
- Clinical Features
  - Unilateral weakness =2 points
  - Speech disturbance without weakness =1 point
- Duration
  - >60 minutes =2 points
  - 10-59 minutes =1 point
- Diabetes =1 point

Aggressive Therapy for TIA

- 1. SOS-TIA trial
  - 1085 patients with TIA admitted to a 24-hour center
  - All treated with standard therapy
    - 74 percent discharged on same day, stroke risk reduced 80 percent from ABCD² prediction
- 2. EXPRESS study
  - 80 percent reduction in risk with urgent TIA clinic visit versus usual primary care visit in 1278 patients

TIA Aggressive Therapy: A Modern Look

- 2009-2011 TIA registry of nearly 5000 patients
- Population at baseline was high risk as with historical cohorts
- 78% saw a stroke specialist within 24 hours
  - Hospitalists not mentioned in this European study
- 1-year stroke rate was 5.1%
- Rates at 2d, 7d, 30d, 90d, 1y were all less than half of that in historical cohorts
When to Fix the Carotid?

- NASCET in early 1990s
  - Benefit of endarterectomy in patients with symptoms ipsilateral to 70-99% stenosis
  - Comparison: best medical management at the time
  - 50-69% symptomatic stenosis revascularization has limited benefit, especially in women
- In stroke management don’t miss carotid disease or atrial fibrillation

How to Fix the Carotid?

- Stenting vs. CEA: CREST Trial
- 4-year study of 1321 symptomatic and 1181 asymptomatic patients randomized to CEA vs. carotid stenting
- Combined endpoint of stroke, MI, death not significantly different
  - More strokes in first 90 days in stenting group, more MIs in surgical group
  - After 90 days, similar endpoints

The High-Yield Neurologic Examination

S. Andrew Josephson MD
Carmen Castro Franceschi and Gladyne K. Mitchell Neurohospitalist Distinguished Professor
Chair, Department of Neurology
Founder, Neurohospitalist Program
University of California, San Francisco

The speaker has no disclosures

Examination Approach

• Two types of neurologic examinations
  – 1. Screening Examination
  – 2. Testing Hypotheses
• Select high-yield tests and techniques

Examination Approach

• Organization
  1. Mental Status
  2. Cranial Nerves
  3. Motor
  4. Reflexes
  5. Sensory
  6. Coordination
  7. Gait

The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

1. If the patient can give a completely coherent history, then the mental status examination is probably normal
**Digits Forward**
- Outstanding test of attention to screen for delirium
- Given successively long strings of digits 1 second apart
  - 6-8-2-4
  - 5-1-9-3-5
  - 8-6-2-6-3-7
  - 5-4-6-9-7-5-2
- Less than 5 is abnormal and indicates an attentional deficit

**Case 1: Mental Status**
- A 73 year-old woman comes to the ER with 2 days of feeling fatigued
- General physical examination is normal and there is no weakness on neurological examination
- Language testing is abnormal

**The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination**

1. If the patient can give a completely coherent history, then the mental status examination is probably normal
2. Speech does not equal language: test three elements of language in each patient

**Aphasia Testing**
- Fluency: Use Naming and Conversation
- Comprehension: More difficult commands
- Repetition: “Today is a sunny day…”
### Aphasia Chart

<table>
<thead>
<tr>
<th>Name</th>
<th>Fluency</th>
<th>Comp</th>
<th>Rep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broca’s</td>
<td>Bad</td>
<td>Good</td>
<td>Bad</td>
</tr>
<tr>
<td>Wernicke’s</td>
<td>Good</td>
<td>Bad</td>
<td>Bad</td>
</tr>
<tr>
<td>Global</td>
<td>Bad</td>
<td>Bad</td>
<td>Bad</td>
</tr>
<tr>
<td>Conduction</td>
<td>Good</td>
<td>Good</td>
<td>Bad</td>
</tr>
<tr>
<td>Transcort Motor</td>
<td>Bad</td>
<td>Good</td>
<td>Bad</td>
</tr>
<tr>
<td>Transcort Sens.</td>
<td>Good</td>
<td>Bad</td>
<td>Good</td>
</tr>
<tr>
<td>Transcort Mixed</td>
<td>Bad</td>
<td>Bad</td>
<td>Good</td>
</tr>
</tbody>
</table>

### Cranial Nerve Testing

- II: Pupils, Acuity, Visual Fields
- III, IV, VI: Extraocular Movements
- V: Facial Sensation
- VII: Facial Strength
- VIII: Hearing
- IX, X: Palatal Elevation and Gag
- XI: SCM and Trapezius Power
- XII: Tongue Power

### The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

1. If the patient can give a completely coherent history, then the mental status examination is probably normal
2. Speech does not equal language: test three elements of language in each patient
3. Visual field testing is highly informative and underutilized by the non-neurologist

### Screening for Visual Field Deficits

- Cooperative patient: Move examiner finger in the center of each quadrant with patient gaze fixed
  - Test each eye by covering the opposite eye, present stimulus in all 4 quadrants
- Uncooperative patient: Use a single digit to suddenly approach each half of the visual fields; normally elicits a blink
  - Avoid using entire hand: elicits corneal reflex
  - Report as “Does/Does not blink to threat”
**Central vs. Peripheral: Vertigo Exam Findings**

- Always central, always needs imaging
  - 1. Any Cranial Nerve Lesion
  - 2. Any Asymmetric Cerebellar Finding
  - 3. Complete Absence of Peripheral Signs

**HINTS**

- Three step screen
  - 1. **Head Impulse** (should perform last)
  - 2. **Nystagmus**
  - 3. **Test of Skew**

---

**Coma**

- Definition:
  - Not Awake
  - Not Arousable
  - Not Aware
4. After establishing new-onset coma, the pupillary examination is the most important initial neurologic examination test.

Two Localizations of Coma

- 1. Brainstem
- 2. Bilateral Hemispheres

Step 1: CN exam to localize to brainstem or hemispheres
Step 2: Pupils uneven: Structural not metabolic etiology

Case 2: Cranial Nerves

- A 54 year-old man with no PMH presents after being hit in the right temple with a baseball while playing with his son.
- General physical exam is normal. On neurologic examination the patient is lethargic. The right pupil is 7mm and minimally reactive while the left reacts briskly 3 to 2mm. The rest of the neurologic examination is normal.

“Fixed” Pupils and Coma

- Dilated (7-9mm): Early Herniation
- Mid-Position (3-5mm): Late Herniation
- Caveats
- ? Adequacy of light stimulus
- ? Drug Effect
Case 2: Cranial Nerves

• Over the next hour, the patient becomes unresponsive and develops extensor posturing on his left side

Cranial Nerve Testing: Coma

II: Pupils, Visual Fields
III, IV, VI: Oculocephalic Maneuver
V, VII: Corneal Reflex
VIII: Cold Calorics
IX, X: Gag, Cough, Spontaneous Respirations

The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

4. After establishing new-onset coma, the pupillary examination is the most important initial neurologic examination test
5. Use an appropriate screen for Upper Motor Neuron-type weakness

Case 3: Motor

• A 75 yo male with HTN, DM and current tobacco use comes to the ED with mild problems walking and a complaint of “my left arm is not working right.”
Case 3: Motor

- The ED physician tells you that he knows the patient has no weakness in his extremities as his own exam shows equal hand grasps, moving all fours, and “stepping on the gas” in the lower extremities.

Upper Motor Neurons of the Pyramidal Tract

Predictable Pattern of Weakness
Distal Extensors of the UEs and Distal (Dorsi)Flexors of the LEs

Quick Screen for Upper Motor Neuron/Pyramidal Weakness

- Pronator Drift
- Fine Finger Movements/Toe Taps
- One muscle in each of four extremities
  - Upper Extremities: 1st DI or finger extensors
  - Lower Extremities: Extensor of big toe
- Common ED screen VERY insensitive!

The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

4. After establishing new-onset coma, the pupillary examination is the most important initial neurologic examination test
5. Use an appropriate screen for Upper Motor Neuron-type weakness
6. Use the exam to localize the weakness in the nervous system
### The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

4. After establishing new-onset coma, the pupillary examination is the most important initial neurologic examination test
5. Use an appropriate screen for Upper Motor Neuron-type weakness
6. Use the exam to localize the weakness in the nervous system
7. Use the sensory examination sparingly and logically, testing each major pathway

### Sensory Testing Modalities

- Vibration (128Hz Tuning Fork)
- Joint Position Sense/Proprioception
- Temperature
- Pinprick
- Light Touch (Not Useful)

---

<table>
<thead>
<tr>
<th>Pattern of Weakness</th>
<th>UMN</th>
<th>LMN</th>
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<tbody>
<tr>
<td>Function/Dexterity</td>
<td>Pyramidal</td>
<td>Variable</td>
</tr>
<tr>
<td>Tone</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Tendon Reflex</td>
<td>Increased</td>
<td>Decreased, absent or normal</td>
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<tr>
<td>Other signs</td>
<td>Babinski sign, other CNS signs (e.g. aphasia, visual field cut)</td>
<td>Atrophy (except with problem of neuromuscular junction)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Weakness Pattern</th>
<th>Motor Neuron Disease</th>
<th>Neuropathy</th>
<th>NMJ</th>
<th>Myopathy</th>
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<tbody>
<tr>
<td>DTR</td>
<td>Variable</td>
<td>Distal</td>
<td>Diffuse</td>
<td>Normal or decreased</td>
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<tr>
<td>Atrophy</td>
<td>Increased, normal and/or decreased</td>
<td>Decreased or absent</td>
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<td></td>
</tr>
<tr>
<td>Fasciculations</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Sensory symptoms/ signs</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensory Testing Modalities</th>
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<tbody>
<tr>
<td>Vibration (128Hz Tuning Fork)</td>
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<td>Joint Position Sense/Proprioception</td>
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<td>Pinprick</td>
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<tr>
<td>Light Touch (Not Useful)</td>
</tr>
</tbody>
</table>
Sensory Testing Modalities
- Vibration (128Hz Tuning Fork)
- Joint Position Sense/Proprioception
- Temperature
- Pinprick

Case 4: Sensory
- A 45 yo man presents with 2 days of progressive tingling and weakness of the lower extremities. He now is having trouble walking and rising from a chair.

Case 4: Sensory
- Exam
  - MS, CN normal
  - Motor: normal tone throughout, normal power in upper ext., 4/5 throughout in the lower extremities
  - Sensory: decreased PP/Vib/temp patchy in lower extremities
    - A sensory level is found at T10

The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination
8. Symmetry of reflexes is important, rather than absolute value
Reflex Tips

• Know the cord level of each reflex
  – Biceps: C5-6
  – Triceps: C7-8
  – Patella: L2-4
  – Ankle: L5-S1
• Symmetric positioning is key
• Expose the muscle being tested
• Strike with only moderate force

Case 5: Coordination

• A 54 year-old woman presents with vertigo and gait difficulties
• On finger-nose-finger, she exhibits dysmetria with the right upper extremity, but not with the left

The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

8. Symmetry of reflexes is important, rather than absolute value
9. In the coordination exam, bilateral abnormalities are often benign

Key Cerebellar Exam Tips

• Bilateral dysfunction is often benign and drug/medication related
• Unilateral dysfunction is a cerebellar lesion until proven otherwise
  – CT insensitive in this region
• Cerebellar tracts run through the brainstem
  – Cerebellar signs with cranial nerve deficits is a brainstem lesion until proven otherwise
The “High-Yield” Neurologic Examination: Top Ten Suggestions for a Better Neurologic Examination

8. Symmetry of reflexes is important, rather than absolute value
9. In the coordination exam, bilateral abnormalities are often benign
10. The single most useful test on the neurologic exam is having the patient ambulate

The (Misunderstood) Romberg

- How to perform
- What systems help us stand?
  - 1. Cerebellum
  - 2. Motor
  - 3. Vestibular
  - 4. Dorsal Columns
  - 5. Vision

Part of the Sensory Exam!
NOT Gait or Coordination Exam

The Quick Screening Exam

1. Mental Status: Digits forward, 3 elements of language
2. Cranial Nerves: Pupils, visual fields, EOMs, facial droop
3. Motor: 3-step screen for UMN weakness
4. Reflexes:
5. Sensory: Test toes w/ 2 modalities (1 from each path); Romberg
6. Coordination: Finger-nose-finger
7. Gait: Walk the patient
Challenging cases of hospitalized patients with cirrhosis

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Associate Professor of Clinical Medicine
Program Director, Transplant Hepatology Fellowship
Inpatient Chief of Service, Hepatology

October 21, 2021

Disclosures
Grant/research support: Gilead, NGM, Genentech

Improving Mortality In Hospitalized Cirrhotic Patients

HEPATOLOGY
PRACTICE GUIDANCE | HEPATOLOGY, VOL 45, NO 4, 2019
Development of Quality Measures in Cirrhosis by the Practice Metrics Committee of the American Association for the Study of Liver Diseases

Sakuntabai Ramkumar,1,2 Steven J. Kowdley,1 Abhishek Roy,1 Yasser R. Rozema,3,4 Nidhi Devadas,1 John P. Rossmeissl,1,5 Angela Haim,1 Yvonne Andrews-Gaye1,2,6 Bruce Lenane,1,6 and Michael S. Sanderson1,2

SCHOOL OF MEDICINE • UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
Tough consult questions

- Beta blockers: what the heck should I do with them?
- My patient is in pain, what do I do?
- My patient has AKI. Is it hepatorenal syndrome?
- Should this patient get a TIPS?
- What can I do for this patient with refractory hydrothorax?
- This patient is admitted with ascites again. Do I really need to tap them?
- Does my patient need a liver transplant?

Case 1

55yo woman with NASH cirrhosis, Child’s class B, with moderate ascites previously controlled on diuretics and hepatic encephalopathy. She has no history of prior variceal bleeding. She undergoes screening endoscopy and is noted to have medium varices. She is started on a nonselective beta blocker for primary prevention of variceal hemorrhage.

6 months later, she is hospitalized with tense ascites and acute kidney injury. What should be done with her beta blocker?
What should happen to a NSBB in a patient with worsening ascites/decompensation?

- Stop the beta blocker
- Switch to a selective beta blocker
- Increase the beta blocker dose
- It depends
- I don’t know, please tell me, that’s why you’re here

Beta blockers may be associated with increased risk of ARI in refractory ascites


No impact of NSBB on survival in patients with ascites

<table>
<thead>
<tr>
<th>Impact of NSBB</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
</tr>
<tr>
<td>Refractory ascites</td>
</tr>
<tr>
<td>Nonrefractory ascites</td>
</tr>
<tr>
<td>Short-term (6-month) mortality</td>
</tr>
</tbody>
</table>
Patients who respond to beta blockers and maintain response (based on portal pressures) have superior survival than those who never respond or lose response to beta blockers.

Survival benefit of beta blockers may be lost in patients with baseline MAP of <65.

MAP and BB response impact survival

- Beta blockers can blunt compensatory increases in cardiac output
- Worsened hypotension in patients with baseline low SVR
- Decreased renal perfusion

What is happening?

Case 1 (cont’d)

55yo woman with NASH cirrhosis, with recent worsening of ascites, hospitalized with tense ascites, rising MELD score, AKI. She is on a NSBB for primary prevention of variceal bleeding.

Diagnostic paracentesis shows evidence of spontaneous bacterial peritonitis (SBP).

Case 1 (cont’d)

55yo woman with NASH cirrhosis, with recent worsening of ascites, hospitalized with tense ascites, rising MELD score, AKI. She is on a NSBB for primary prevention of variceal bleeding.

Diagnostic paracentesis shows evidence of spontaneous bacterial peritonitis (SBP).

Now what should be done with her beta blocker?
What should you do with a NSBB in a patient with SBP?

1. Stop the beta blocker during hospitalization
2. Switch to a selective beta blocker
3. Increase the beta blocker dose
4. I don’t know, please tell me, that’s why you’re here

Beta blockers reduce risk of developing SBP

<table>
<thead>
<tr>
<th>n</th>
<th>Child A/B/C (%)</th>
<th>Ascites (%)</th>
<th>Follow-up (months)</th>
<th>SBP BB vs control (%)</th>
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<tbody>
<tr>
<td>Burns AJG, 2006</td>
<td>71</td>
<td>83/17/0</td>
<td>35</td>
<td>76</td>
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<tr>
<td>Gonzales-Suarez Eur J Gastroenterol Hep, 2006</td>
<td>230</td>
<td>22/57/21</td>
<td>64</td>
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<td>Abraldes Hepatology 2003</td>
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<td>Hoshino AJG 2000</td>
<td>139</td>
<td>--</td>
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<td>96</td>
</tr>
</tbody>
</table>

Beta blockers increase risk of death after first episode of SBP

p = 0.089
Beta blockers increase risk of HRS/AKI after first episode of SBP

- Patients treated with beta blockers were sicker
  - More often Child’s C cirrhosis (67 vs 53%)
  - Higher bilirubin (5 vs 3)

Summary: NSBB

- Beta blockers may have deleterious effects in cirrhosis
  - Poorer survival in patients with refractory ascites
  - Increased risk of HRS/AKI in SBP
  - Some of the effects of beta blockers observed may be due to sicker patients treated with beta blockers
  - Beta blocker effect may vary over time
    - Discontinuation or nonadherence due to side effects
    - Loss of response over time
- No RCT level data to help guide decision making in decompensated cirrhosis
Take home points: NSBB

- Consider stopping NSBB in patients with refractory ascites if they have:
  - Systolic blood pressure <90mmHg or MAP <65
  - Na <130 and/or Cr >1.5
  - No history of variceal bleeding or large varices
  - Stop NSBB during a hospitalization for SBP
- Consider limiting NSBB dose to:
  - Propranolol <120mg/day
  - Nadolol <80mg/day

Case 1 (cont’d)

55yo woman with NASH cirrhosis, hospitalized with tense ascites, rising MELD score, and AKI, found to have SBP.

She reports problems with abdominal pain that is preventing her from sleeping and ambulating.

How should you manage her pain?

A. Ibuprofen
B. Hydrocodone/acetaminophen
C. Oxycodone
D. Acetaminophen
E. Did you really include acetaminophen as an option? That’s crazy talk.
How should you manage pain in a patient with decompensated cirrhosis?

A. Ibuprofen  
B. Hydrocodone/acetaminophen  
C. Oxycodone  
D. Acetaminophen  
E. Did you really include acetaminophen as an option? That's crazy talk.

Challenges of pain management in cirrhosis

PATIENT
- Metabolic comorbidities
- Substance use disorders
- Psychiatric disease
- Low socioeconomic status / health literacy

PHARMACOLOGIC
- Impaired hepatic metabolism
- No biomarkers to measure hepatic function
- Impaired renal excretion
- Risk for adverse effects
- Renal failure
- Hepatic encephalopathy
- Potential for abuse

CLINICIAN
- No guidelines
- Discomfort with analgesic options
- Stigma/bias

DISEASE
- Variable presentations
- Minimal research on cirrhosis-related pain

SYSTEM
- Regulatory issues
- Transplant center requirements
- Fragmentation of care


How is pain managed in cirrhosis?

Acetaminophen (APAP) is the leading cause of drug-induced liver injury in the US

- This occurs when APAP is taken above recommended limits (4g/day in patients without liver disease)
- Upper limit of APAP in chronic liver disease = 2 grams/day
- Potential for decreased metabolism of APAP
- Chronic alcohol use depletes glutathione stores, thereby lowering the threshold for APAP toxicity
- Combination opioid/APAP formulations may be high risk due to habituation to opioid component leading to escalating use and increased APAP intake

Myth: patients with cirrhosis can't take acetaminophen
NSAIDs are high risk in cirrhosis
- Acute kidney injury
  - Prostaglandin inhibition reduces renal perfusion
  - Higher risk in patients with ascites on diuretics
- Gastrointestinal bleeding risk
  - Gastric mucosal injury
  - Decreased platelet aggregation due to thromboxane inhibition

Opioid impact on morbidity and mortality
- Mechanisms that impact hepatic encephalopathy (HE)
  - Decreased metabolism and clearance
  - Increased brain sensitivity to opioids in patients with HE
  - Decreased gut motility
- Outcomes
  - Increased risk of (all cause) hospitalization
  - Post-transplant outcomes in pre-transplant opioid users
    - Poorer graft survival
    - Increased hospitalizations

Take home points:
Pain management in cirrhosis
- Acetaminophen is the safest pain reliever in patients with cirrhosis
  - Limit intake to <2g/day
- Avoid NSAIDs, particularly in patients with ascites
- Avoid opioids, particularly in patients with hepatic encephalopathy

Wait, what about the AKI?
55yo woman with NASH cirrhosis, hospitalized with tense ascites, rising MELD score, and AKI, found to have SBP.
Labs: Cr 2.87, Na 130, WBC 5, hct 32, plt 83, INR 2.0, tibi 7, albumin 2.7
Baseline Cr 0.5
Wait, what about the AKI?

55yo woman with NASH cirrhosis, hospitalized with tense ascites, rising MELD score, and AKI found to have SBP.

Labs: Cr 2.87, Na 130, WBC 5, hct 32, plt 83, INR 2.0, bilirubin 7, albumin 2.7
Baseline Cr 0.5

So, does she have hepatorenal syndrome? What do I do about it?

What are the next steps in evaluation of AKI in this patient?

- This is hepatorenal syndrome. Start midodrine and octreotide.
- The patient is volume overloaded. Increase diuretics.
- Hold diuretics, give IV albumin, diagnostic paracentesis
- Continue diuretics, give IV NS, diagnostic paracentesis
- Hold diuretics, give IV albumin, diagnostic paracentesis

AKI in cirrhosis
International Ascites Club criteria

<table>
<thead>
<tr>
<th>Subject</th>
<th>Definition</th>
</tr>
</thead>
</table>
| Baseline sCr     | sCr obtained within 3 months prior to admission  
|                  | • If >1 value within the previous 3 months, the value closest to the admission  
|                  | • If no previous sCr, the sCr on admission should be used  |
| Definition of AKI| Increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) within 48 hours, or  
|                  | Increase sCr ≥50% within the prior 7 days  |

- AKI as defined is associated with ICU transfer, longer hospital stay, and increased in-hospital and 90-day mortality
**Management of AKI**
- Investigate non-HRS causes:
  - Review medication history: diuretic dose change or initiation, NSAIDs or other nephrotoxic drugs, iodinated contrast
  - Urinalysis with microscopy
  - Renal ultrasound
  - Evaluate for infection
  - Administer volume expansion: IV albumin 1g/kg (using 25% albumin) x 2 days

**Hepatorenal syndrome (HRS)-AKI**
- Cirrhosis with ascites
- AKI as defined by ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and volume expansion
- Absence of shock
- No nephrotoxins
- No signs of structural kidney injury
  - Urine protein <500mg/day
  - No microscopic hematuria
  - Normal renal ultrasound

**Treatment of hepatorenal syndrome**
- Vasoconstriction of systemic and splanchnic circulation to improve effective circulating volume and renal perfusion
  - Oral: midodrine
  - IV/SQ
    - Octreotide 100-200mcg SQ TID (with midodrine)
    - Norepinephrine: requires ICU level of care or special floor protocol
    - Terlipressin: not approved for use in the US
  - Albumin dose of 40-50g/day

**AKI progression is associated with illness severity and survival**

**International Ascites Club Criteria**
- Cirrhosis with ascites
- AKI as defined by ICA-AKI criteria
- No response after 2 consecutive days of diuretic withdrawal and volume expansion
- Absence of shock
- No nephrotoxins
- No signs of structural kidney injury
  - Urine protein <500mg/day
  - No microscopic hematuria
  - Normal renal ultrasound
Management of AKI in cirrhosis

Acute rise in Cr by >0.3 above baseline

Evaluate for precipitants of AKI

Non-HRS cause

No dx identified

Hold diuretics

Cr >0.3 above or 1.5-2x baseline Cr

No improvement

IV albumin x 2 days

No improvement

HRS criteria met

Treat for HRS

Should my patient get a TIPS?

Which patient(s) is (are) candidates for TIPS?

- 57F with refractory ascites, MELD 32
- 57F with refractory ascites, MELD 16
- 43M with large varices on routine endoscopy, platelet count 43, MELD 15
- 43M admitted with variceal bleeding, Child’s B cirrhosis
- A&C
- B&D
- All of the above

Which patient(s) is (are) candidates for TIPS?

- 57F with refractory ascites, MELD 32
- 57F with refractory ascites, MELD 16
- 43M with large varices on routine endoscopy, platelet count 43, MELD 15
- 43M admitted with variceal bleeding, Child’s B cirrhosis
- A&C
- B&D
- All of the above
Case 3a
- 57F with cirrhosis due to autoimmune hepatitis with refractory ascites.
- She has been getting therapeutic paracentesis for the past 4 months, and the frequency has now increased to every 5 days, with removal of 8-10L each time
- She is hospitalized frequently due to intermittent problems with volume overload, AKI, and/or hyponatremia
- Labs: INR 1.5, Na 136, Cr 1.1, tbili 2.2, MELD-Na 16

TIPS confers survival benefit over serial paracentesis

Predictors of mortality

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIPS</td>
<td>0.61</td>
<td>0.41-0.91</td>
</tr>
<tr>
<td>Age</td>
<td>1.024</td>
<td>1.001-1.048</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>1.22</td>
<td>1.061-1.40</td>
</tr>
<tr>
<td>Sodium</td>
<td>0.95</td>
<td>0.92-0.99</td>
</tr>
</tbody>
</table>

LT-free Survival

TIPS vs. serial paracentesis

- Incidence of hepatic encephalopathy is similar between TIPS vs paracentesis groups, though severe HE may be more common with TIPS

TIPS vs. serial paracentesis

- Incidence of hepatic encephalopathy is similar between TIPS vs paracentesis groups, though severe HE may be more common with TIPS

<table>
<thead>
<tr>
<th>Complication</th>
<th>TIPS</th>
<th>LVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>15%</td>
<td>28%</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>8%</td>
<td>13%</td>
</tr>
<tr>
<td>SBP</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>HRS</td>
<td>5%</td>
<td>13%</td>
</tr>
</tbody>
</table>
Contraindications to TIPS

<table>
<thead>
<tr>
<th>Relative</th>
<th>Absolute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatocellular carcinoma, especially centrally located</td>
<td>Primary prevention of variceal bleeding</td>
</tr>
<tr>
<td>Obstruction of all liver veins</td>
<td>Compensatory heart failure</td>
</tr>
<tr>
<td>PV thrombosis</td>
<td>Severe tricuspid regurgitation</td>
</tr>
<tr>
<td>Moderate pulmonary hypertension</td>
<td>Severe pulmonary hypertension</td>
</tr>
<tr>
<td>Severe coagulopathy (international normalised ratio &gt;3)</td>
<td>Multiple hepatocysts</td>
</tr>
<tr>
<td>Thrombocytopenia of &lt;20,000 cells/µL</td>
<td>Uncontrolled systemic infection or sepsis</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td></td>
</tr>
</tbody>
</table>

MELD >15-18 and/or total bilirubin >3

Case 3b
- 43yo man with alcohol related cirrhosis who is hospitalized with hematemesis
- Recent onset ascites and jaundice
- VS: HR 120 BP 95/63 RR 20 SpO2 95%
- Gen: uncomfortable, lethargic, hematemesis in ED
- Abd: distended, bulging flanks, mildly uncomfortable to palpation but no peritoneal signs. + melena stool
- Labs: WBC 4, Hb 5.7, plt 80, INR 1.6, Na 136, Cr 0.9, total bil 4.3, albumin 2.9, CP C10, MELD Na 18
- Intubated for airway protection, 2 PIVs, transfused 2u pRBCs, protonix gtt, octreotide gtt, ceftriaxone
- Urgent EGD shows actively bleeding EVs

Take home points
- TIPS has a survival benefit in patients with refractory ascites and select patients with variceal bleeding
- If you are considering TIPS, you should also be considering referral for liver transplant evaluation
- Pre-TIPS checklist:
  - TTE to rule out heart failure and pulmonary hypertension
  - CT to evaluate hepatic vasculature

Early TIPS in variceal bleeding
- Greatest benefit in Child's C cirrhosis in this RCT
- Several studies (not meta-analysis) show similar findings supporting use of pre-emptive TIPS
57F with NASH cirrhosis is hospitalized for the 4th time in 2 months with shortness of breath. She has a history of hepatic hydrothorax that has gotten progressively worse over time. She undergoes therapeutic thoracentesis now twice weekly, with 1-2L fluid removed each time. She is frustrated with her frequent hospitalizations and poor quality of life. Diuretic doses have been increased to the highest tolerable dose, with higher doses associated with AKI, hyponatremia, and/or hyperkalemia in the past.

Quickfire Case 1

VS: T36.4 HR 73 BP 109/53 RR 24 SpO2 95%
Gen: chronically ill
Resp: Decreased breath sounds throughout all lung fields on the right
Labs: WBC 6, hct 28, plt 51, INR 1.4, Na 134, Cr 1.02, total bili 2, albumin 2.7, MELD-Na 16

QC1: What is the best treatment option available to this patient with refractory hepatic hydrothorax, MELD-Na 16?
A. Pleurex catheter insertion
B. Serial therapeutic thoracentesis
C. TIPS
D. Pleurodesis
QC1. What is the best treatment option available to this patient with refractory hepatic hydrothorax, MELD-Na 16?

A. Pleurex catheter insertion
B. Serial therapeutic thoracentesis
C. TIPS
D. Pleurodesis

TIPS and hepatic hydrothorax
- Response rates: 59-82%
- Mortality
  - 30-day: 5-25%
  - 1-year: 36-52%

Pleural catheter for HH
- Attractive option for patients who need frequent thoracentesis or who are at higher risk of bleeding
- May result in spontaneous pleurodesis in 33%
- Risk of complications: 36%
  - 10-16% SBE
  - Deaths typically due to sepsis
- If used as a bridge to transplant, plan should be made in conjunction with transplant team

Patients with HH are at high risk of death regardless of management
Quickfire Case 2

47M with alcohol related cirrhosis is brought into the ED with altered mental status. He had been taking lactulose as prescribed, but his family notes that he has not had a bowel movement in the past 24 hours.

VS: T36.7, HR 80, BP 117/62, RR 12, SpO2 99%
Gen: chronically ill, muscle wasting
Neuro: Unarousable to verbal stimuli, occasionally grunts in response to deep physical stimuli. Oriented x 0. +clonus

Labs: WBC 5, hct 33, plt 95, INR 1.9, Na 136, Cr 0.97, total bili 4.7, albumin 2.6

QC2. What are your next steps for management of severe HE?

A. Check ammonia. Titrate lactulose dose according to serial ammonia levels
B. Intubate. Place feeding tube for frequent administration of lactulose and rifaximin +/- PEG. Adjust dose according to mental status and stool output
C. Give flumazenil
D. Intubate. Use midazolam for sedation. Administer lactulose PR
Management of hepatic encephalopathy (HE)

**Overt HE**
- Triage to appropriate level of care
- Intubate if needed
- Lactulose* and rifaximin per NGT/FT, titrate to mental status
- Rifaximin

- Evaluate and treat precipitants
  - Infection
  - GI bleeding
  - AKI/hypovolemia
  - Sedating meds
  - Medication nonadherence

- Non-severe HE

- Lactulose PO, titrate to mental status
- Add rifaximin if not already taking

- Severe HE

- If no improvement in 24 hrs
  - Add zinc sulfate
  - CT head +/- neuro consult
  - Evaluate for PS shunt

Continue maintenance therapy once HE resolves

*or PEG

Rifaximin reduces hospitalization and its use is cost-effective

- Rifaximin reduces episodes of breakthrough HE, need for HE-related hospitalization, and length of hospitalization
- Numerous studies have demonstrated cost-effectiveness of rifaximin

Coordination of care after HE hospitalization

- ~40-50% of patients discharged after a hospitalization for HE may not fill prescriptions for HE meds, in part related to medication cost (rifaximin >>>> lactulose)
- Measures should be taken to ensure patients can access rifaximin after hospital discharge
- Patients and families should be educated about HE management
What about ammonia levels?

Ammonia levels have no impact on HE outcomes

Quickfire Case 3

- 55F with NASH cirrhosis with a history of ascites on diuretics, presents to the emergency department with complaints of abdominal pain and increasing distension.
- Ascitic fluid analysis from paracentesis in 2018 and 2019 showed high SAAG and low total protein.
- VS: T37 HR 65 BP 110/70 RR 20 SpO2 98%
- Gen: chronically ill, slightly uncomfortable due to abdominal distension
- Resp: normal other than decreased BS at bases
- GI: tensely distended abdomen with dullness to percussion, nontender
- Neuro: AAOx3, no asterixis
- Labs: WBC 5, hct 30, plt 55, INR 2.3, Na 130, BUN 53, Cr 1.6, total bili 5, albumin 3.0

QC3a. What are your next steps for evaluating worsening ascites?

- Diagnostic paracentesis, with fluid sent for culture in blood culture bottles
- Diagnostic paracentesis, with fluid sent for culture in a sterile tube
- No need for paracentesis, there is no abdominal tenderness, fever, nor leukocytosis
- Arrange for urgent TIPS
QC3a. What are your next steps for evaluating worsening ascites?

A. Diagnostic paracentesis, with fluid sent for culture in blood culture bottles
B. Diagnostic paracentesis, with fluid sent for culture in a sterile tube
C. No need for paracentesis, there is no abdominal tenderness, fever, nor leukocytosis
D. Arrange for urgent TIPS

Evaluation of ascites

*Serum ascites albumin gradient (SAAG) = serum ascites – albumin ascites

SCHOOL OF MEDICINE | UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
### Diagnostic paracentesis

<table>
<thead>
<tr>
<th>Test</th>
<th>1st paracentesis</th>
<th>Subsequent paracentesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAAG</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cell count w/ diff</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Culture</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Protein</td>
<td>Yes</td>
<td>May*</td>
</tr>
<tr>
<td>Glucose</td>
<td>Only as driven by clinical suspicion (e.g., no cirrhosis, secondary peritonitis, malignancy, pancreatitis)</td>
<td></td>
</tr>
<tr>
<td>Cytology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amylase</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If needed to determine primary SBP prophylaxis and/or concerned about secondary peritonitis

---

### QC3b. When should I do paracentesis on this patient?

- Within 4 hours of admission
- Within 1 day of admission
- I told you I’m not doing paracentesis, there is no abdominal tenderness, fever, nor leukocytosis
- Whenever IR can do the procedure
Spontaneous bacterial peritonitis (SBP)

- ~30% of patients with SBP may lack typical signs/symptoms of fever, abdominal pain, and/or leukocytosis
- Diagnosis: 250 PMNs/mm³
- Prognosis
  - In-hospital death: 10-20%
  - Median survival: 6 months
  - Recurrent SBP: 40-70% at 1 year

Quickfire Case 3 (cont’d)

- 55F with NASH cirrhosis presents to the emergency department with complaints of abdominal pain and distension
- Paracentesis with removal of 5L amber fluid
- WBC 893 (75% PMNs), RBC 100
- Albumin 1.0, total protein 1.2
- Cultures pending

QC3b. What are your next steps in management?

A. Supportive care. Wait to start antibiotics until culture results return
B. Treat for SBP with vancomycin.
C. Arrange for urgent TIPS
D. Treat for SBP with ceftriaxone. Give 1.5g/kg IV albumin on day 1, 1g/kg IV albumin on day 3
Prevention of HRS in SBP

- RCT of 126 patients with SBP treated with cefotaxime, albumin vs no albumin
  - 1.5g/kg on day 1, 1g/kg on day 3

Impact may be greatest in patients with Cr>1, BUN>30, and/or tbili >4

<table>
<thead>
<tr>
<th>Albumin</th>
<th>Control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal impairment</td>
<td>10%</td>
<td>33%</td>
</tr>
<tr>
<td>Death</td>
<td>10%</td>
<td>22%</td>
</tr>
<tr>
<td>In hospital</td>
<td>29%</td>
<td>41%</td>
</tr>
<tr>
<td>3 months</td>
<td>29%</td>
<td>41%</td>
</tr>
</tbody>
</table>

QC4. Which patient(s) should you refer for liver transplant evaluation urgently?

- 35M with alcohol associated cirrhosis with 3 months sobriety, refractory ascites, AKI/HRS, MELD 32
- 53F with NASH cirrhosis, BMI 41, DM, frequent admissions for AKI and/or HE, MELD 32
- 71M with cirrhosis due to HBV + NASH, acute decompensation from HBV flares, MELD 37. Working full time and exercising regularly right before hospitalization
- 65F with cirrhosis due to autoimmune hepatitis, CKD stage 3, worsening liver failure and AKI on CKD after variceal bleeding, MELD 31
- All of the above

Narrow window for LT in acute on chronic liver failure (ACLF)

Cases or questions from the audience

Thank you!

Danielle.Brandman@ucsf.edu
Objectives

- Lingering questions from this mornings presentations
- Duration of anticoagulation for VTE
- Approach to subsegmental PE, calf vein DVT and superficial vein thrombosis
- Role of thrombophilia work up
- Resuming anticoagulation after a bleed

Resources

- University of Washington Anticoagulation http://depts.washington.edu/anticoag/home

Case

51 year old man with no PMHX presents with acute CP and SOB, BP stable, HR 120s O2 sat 92%, d-dimer 1500, CT PE with bilateral PE in all lobes with RV/LV ratio > 1.0. BNP 370, trop 1.5. He is started on rivaroxaban. He has no identifiable provoking factors. How long should he remain on anticoagulation?

1) At least 3 months
2) One year
3) Forever
**ESC PE Guidelines—Duration of Therapy**

<table>
<thead>
<tr>
<th>Indication</th>
<th>CHEST 2019</th>
<th>AC Forum 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st provoked VTE</td>
<td>3 mo</td>
<td>3 mo (surgical)</td>
</tr>
<tr>
<td>1st unprovoked VTE</td>
<td>Extended*</td>
<td>Extended</td>
</tr>
<tr>
<td>2nd unprovoked VTE</td>
<td>Extended*</td>
<td>Extended</td>
</tr>
</tbody>
</table>

*Unless risk factors for recurrence persist

ESC: Suggest indefinite

**Duration of Anticoagulation for VTE:**

2016 CHEST and AC Forum Guidelines/Guidance

- Indication
  - CHEST 2019
  - AC Forum 2016
  - clot-related
  - 3 mo
  - 3 mo (surgical)
  - extended

**VTE and Bleeding Risk: 2016 CHEST Guideline**

<table>
<thead>
<tr>
<th>Risk of Major Bleeding After 3 Mo of Anticoagulation, %/y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0 risk factors)</td>
</tr>
<tr>
<td>Baseline risk</td>
</tr>
<tr>
<td>Increased risk</td>
</tr>
</tbody>
</table>

**Risk Factors for Bleeding with Anticoagulation**

- Age >75 y
- Previous bleeding
- Cancer
- Renal or hepatic failure
- Thrombocytopenia
- Prior stroke
- NSAID use
- Anemia
- Alcohol abuse
- Recent surgery
- Recent hospitalization
- Anticoagulation control
CHEST 2021—suggest reduced dose DOAC over full dose for extended phase anticoagulation

\[ \text{Agnelli et al. NEJM 2013} \]

8.8%

4.4%

1.5%

1.2%


4.4%

1.5%

1.2%

\[ \text{CHEST 2021—suggest reduced dose DOAC over full dose for extended phase anticoagulation} \]

\[ \text{Agnelli et al. NEJM 2013} \]

\[ \text{Weitz et al. N Engl J Med March 2017} \]

UNPROVOKED VTE

- All - 3-6 months of FULL intensity anticoagulation
  - At 3-6 months determine candidacy for secondary prevention
  - ~50% will develop recurrent VTE in 10 years off anticoagulation; Case fatality rate of VTE is ~4% in all comers but closer to 9% in PE
  - Case fatality rate of bleeding is ~10%
  - Case by case decision...consider continuation if not high bleeding risk. Most compelling in low bleed risk patients and in those with PE

\[ \text{Secondary Prevention Options} \]

- Low dose DOAC
- Full dose anticoagulation
- ASA

\[ \text{Secondary Prevention Options} \]

- Low dose DOAC
- Full dose anticoagulation
- ASA

\[ \text{Do not use dose reduced DOAC:} \]

- Cancer
- Recurrent VTE or AC
- Obesity

\[ \text{Do not use dose reduced DOAC:} \]

- Cancer
- Recurrent VTE or AC
- Obesity

**Case**

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Subsegmental PE

A 77 yo man had undergone colectomy for recurrent bleeding from diverticulosis. On POD #3 he becomes tachycardic to the 110s. WBC is elevated. The surgical team orders an abdominal CT which shows a fluid collection concerning for early abscess. It also shows an isolated RLL subsegmental PE. A dedicated CTa shows a single isolated RLL subsegmental PE. Do you anticoagulate this patient?

a) Sure, it is a PE.
b) No this is incidental. Let’s pretend we don’t know it is there.

Isolated Subsegmental PE

Definition: PE shown on CT angiography that occurred in a subsegmental branch but no larger order of vessels. The subsegmental PE may involve one or more than one subsegmental branch.

Identification of ISSPE has tripled over past decade.

Isolated Subsegmental PE

Anticoagulant treatment for subsegmental pulmonary embolism

Summary of main results:

There is currently no evidence from randomised controlled trials to assess the effectiveness and safety of anticoagulation therapy versus no intervention in patients with isolated subsegmental pulmonary embolism (ISSPE) or incidental ISSPE.

IS IT REAL?

ISSPE is more likely to be TRUE if... good quality scan, multi defects, centrally located, d-dimer elevated, seen on multi cuts, patient symptomatic vs incidental, high pretest prob of PE.

Get u/s of bilateral lower extrem (upper if CVC)

Consider risk of recurrence—higher if not post op; immobile; active cancer

IF high bleed risk—don’t AC; get serial u/s.

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A 67 year old man with cirrhosis, new diagnosis of HCC is admitted with diarrhea, lowish BP and AKI. On exam he has bilateral lower extremity swelling, R> L. In the ED he has an ultrasound which shows thrombosis of the greater saphenous vein extending from the calf proximally and terminating 6 cm from the deep femoral vein. What do you recommend?

a. Prophylactic fondaparinux
b. Prophylactic rivaroxaban
c. Full dose DOAC or warfarin
d. Full dose LMWH
e. Warm compresses, no anticoagulation

Factors that favor the use of AC:
- extensive SVT; above the knee, close to saphenofemoral junction;
- severe symptoms; involvement of the greater saphenous vein; history of VTE or SVT; active cancer; recent surgery
- In patients with superficial vein thrombosis of the lower limb of at least 5 cm in length, we suggest the use of a prophylactic dose of fondaparinux or LMWH for 45 days over no anticoagulation (Grade 2B).


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Superficial Vein Thrombosis

A 67 year old man with cirrhosis, new diagnosis of HCC is admitted with diarrhea, lowish BP and AKI. On exam he has bilateral lower extremity swelling, R> L. In the ED he has an ultrasound which shows thrombosis of the greater saphenous vein extending from the calf proximally and terminating 6 cm from the deep femoral vein. What do you recommend?

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Superficial Vein Thrombosis –CHEST Guidelines

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Superficial Vein Thrombosis

Prevention of thromboembolic complications in patients with superficial-vein thrombosis given rivaroxaban or fondaparinux: the open-label, randomised, non-inferiority SURPRISE phase 3 trial

- >400 pts symptomatic SVT riva 10 mg v fonda 2.5mg
- Symptomatic above the knee SVT of at least ≥5 cm length + other risk factor (>65, male, hx VTE, cancer, autoimmune disease, non-varicose veins)
- No difference in primary efficacy outcome
- After 6 weeks 7% recurrence risk in high risk patients (v 1.2% in CALISTO)

A 67 year old man with cirrhosis, new diagnosis of HCC is admitted with diarrhea, lowish BP and AKI. On exam he has bilateral lower extremity swelling, R> L. In the ED he has an ultrasound which shows thrombosis of the greater saphenous vein extending from the calf proximally and terminating 6 cm from the deep femoral vein. What do you recommend?

a. Prophylactic fondaparinux
b. Prophylactic rivaroxaban
c. Full dose DOAC or warfarin
d. Warm compresses, no anticoagulation
50 year old man presents with unprovoked PE. He is hemodynamically stable but CT PE shows elevated RV/LV ratio. ECHO is ordered. He is admitted and started on rivaroxaban. Should you send a work up for thrombophilia?

- Yes—why not, he is here.
- No—then I am going to have interpret it and who needs that.

Thrombophilia Testing

No current guidance/guidelines

EXCEPT ASH Choosing Wisely Campaign—“do not test in provoked VTE”

Results of thrombophilia testing should RARELY affect clinical decisions about VTE treatment—no strong influence on recurrence risk beyond stratification based on clinical presentation

Can help explain “why”
Can be of interest to family members
Current tests are insufficient for identifying inherited VTE risk

Who should we suspect harbors thrombophilia?

- PROTEIN C, S, ANTITHROMBIN DEFICIENCY—OFTEN POSITIVE FAMILY HISTORY
- FACTORY LEIDEN MUTATION AND PROTHROMBIN GENE MUTATION—Northern European descent
- APLS—PRIMARY OR SECONDARY (lupus)
- MAY THURNERS SYNDROME—ILIAC VEIN COMPRESSION SYNDROME...LEFT LOWER EXTREM VENOUS COMPRESSION—LEFT ILIAC VEIN COMPRESSED BY RIGHT ILIAC ARTERY
- UPPER EXTREMITY DVT—PAGET SCHROEDERS SYNDROME—THORACIC OUTLET SYNDROME WITH VENOUS COMPRESSION
- NEPHROTIC SYNDROME/IBD/PNH
- PREGNANCY, IVF
- CANCER (less likely < 50 yo)
VENOUS AND ARTERIAL THROMBOSIS

- APLS
- PFO-with paradoxical embolism
- HYPERHOMOCYSTINEMIA
- SICKLE CELL
- P VERA
- PNH
- HIT
- CANCER
- DIC
- Beurgers disease
- Hyperviscosity-MGUS, MM

Thrombophilia Tests

- Splanchnic vein thrombosis
- Cerebral vein thrombosis
**Antiphospholipid Antibody Syndrome**

- **WHY** - risk of recurrence off AC much higher; at risk for arterial disease, bridge therapy; DOACs generally avoided
- **WHO** - arterial and venous events, unexpected arterial events, recurrent thrombosis ON anticoagulation, underlying autoimmune d/o, prolonged aPTT
- **WHAT** - send Lupus anticoagulant, Beta 2 glycoprotein antibodies and anticardiolipin antibodies (IgG & Ig M)
- **WHEN** - LAC - don't do it on anticoagulation; antibodies you can send anytime
- **IF POSITIVE** -
  - must repeat in 12 weeks - high rate of transient positivity
  - LAC most predictive of 1st and recurrent VTE, triple positives at highest risk

**Thrombophilia Testing**

50 year old man presents with unprovoked PE. He is hemodynamically stable but CT PE shows elevated RV/LV ratio. ECHO is ordered. He is admitted and started on rivaroxaban. Should you send a work up for thrombophilia?

- Yes - why not, he is here.
- No - then I am going to have interpret it and who needs that
What To Do After the Bleed

76 y/o man with CAD (NSTEMI 2006), AFIB CHADS-Vasc=4 on warfarin and ASA is admitted with UGIB. INR is 3.0. He requires 3u PRBCs, vit K and FFP. EGD shows peptic ulcer disease. He is started on high dose PPI therapy, bx for H Pylori done. When should his anticoagulation be restarted?

a) Never
b) In two weeks
c) In three months
d) Let the primary provider deal with this one
"IN THE EVENT OF GI BLEED WE SUGGEST WAITING AT LEAST 7 DAYS WITHOUT EVIDENCE OF ACTIVE BLEEDING AND AFTER ENDOSCOPIC TX BEFORE REINITIATING AC"
Resumption of DOACs

Anticoagulation FULLY therapeutic within 1-2 hours

Only dabigatran has a reversal agent

Considerations After GIB on AC

- Reassess risk benefit of anticoagulation
  secondary prevention of VTE therapy, low CHADS-vasc
- Assess risk of rebleeding from source
  identifiable source, treatable lesion?
- Take steps to decrease risk of bleeding related to AC regimen
- Reconsider need for antiplatelet therapy
  if warfarin was INR in range, is control good?
  spurious elevation in INR or poor TTR → DOAC
  increase INR monitoring → home POC INR?
- If ongoing strong indication for AC determine
  best time to restart therapy in multidisciplinary meeting with proceduralist - Remember DOAC immediately active

What To Do After the Bleed

76 y/o man with CAD (NSTEMI 2006), AFIB CHADS-
Vasc=4 on warfarin and ASA is admitted with UGIB, INR
is 3.0. He requires 3u PRBCs, vit K and FFP. EGD shows
peptic ulcer disease. He requires PPI therapy, bx for H Pylori.
Low CHADS-Vasc=3. What should his anticoagulation be?
a) Never
b) In two weeks
c) In three months
d) Let the primary provider deal with this one

Questions?

“Two weeks may provide the best balance among GI bleed recurrence, thromboembolism and mortality”

Tracy Minichiello, MD
Tough Problems in Inpatient Pulmonary Disease

LEKSHMI SANThOSH, M.D., M.A.ED.

10/21/2021
MANAGEMENT OF THE HOSPITALIZED PATIENT
SMALL GROUP WORKSHOP

Introductions & Ground Rules

- I want to create a fun, casual, engaging environment – both in-person & over Zoom! I will try to engage the audience in this hybrid era.
- Please introduce yourself when you are engaging w/ the speaker so that we can all get to know each other.
- If you are virtual, we are mindful of barriers to turning video on, however, if you have the capacity to do so, we encourage you to ‘show your face’ so we can see each other – not required.
- Feel free to use the chatbox which I will keep an eye on or the Raise Hand function of Zoom.
- Please mute yourself 😊.
- We’re all here to learn & have fun so please enjoy our cases!

Disclosures

None.
### Choose Your Own Adventure! Top 6 Cases

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
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### And of Course the COVID-19 Case!

### Choose Your Own Adventure: Let’s Vote!

A. Could this be VAPI?  
B. It’s not Easy Being Wheezy  
C. Effusion Confusion  
D. A Tickle to the Throat  
E. An International Enigma  
F. Potatoes, Pot-ah-toes  
G. And of course the COVID-19 Case!
Case: Mrs. S

- **Patient:** 57 year old woman with suspected COVID-19 pneumonia presents to the hospital with shortness of breath and fever
- **Review of Systems:** + loss of smell/taste, headaches, decreased appetite for 1 week, previously healthy, no sick contacts
- **Exam:** SpO2 84% on RA, bilateral rhonchi, HR 100, RR 25, BP 133/90
- **Diagnostics:** CXR with mild infiltrates

Q1: What PPE should you wear for patient exam?

1. Surgical
2. Surgical
3. Surgical

Audience Response Q: Click 1, 2, or 3!

Choice A is correct

**Contact and droplet precautions** by health workers caring for suspected and confirmed COVID-19 patients. Surgical facemask at minimum, N95 or higher respirators are preferred if available.
Case: Mrs. S

- **Patient:** 57 year old woman with suspected COVID-19 pneumonia presents to the hospital with shortness of breath and fever
- **Review of Systems:** + loss of smell/taste, headaches, decreased appetite for 1 week, previously healthy, no sick contacts
- **Exam:** SpO2 84% on RA, bilateral rhonchi, HR 100, RR 25, BP 133/90
- **Diagnostics:** CXR with mild infiltrates

Quick Q

You start her on 2 L NC but she quickly desaturates and requires 6 L NC to keep O2 saturation up. You closely monitor her work of breathing and SaO2 and note that she continues to desaturate, but appears comfortable without tachypnea.

Quick Q: Which oxygen delivery device?

1. NC
2. Face Mask
3. Venturi Mask
4. Non-Rebreather
5. HFNC
6. CPAP & NIPPV
7. Ventilator

Audience Response Q
Case (Continued)

- Your patient is started on NRB mask at 15 LPM for decreasing saturations
- With this SpO2 increases to 94%
- RR 27 BPM, patient feels comfortable
- Chest X-Ray worse bilateral infiltrates
- Over next 24 hours SpO2 decreases to 88%
- Patient remains awake and comfortable

Audience Response Q

- Which of the following is the most appropriate next step?
  a. Proning
  b. Intubation
  c. Paralysis
  d. BiPAP

Case (Continued)

- A trial of awake prone positioning is performed
- SpO2 increases to 95% when patient lies prone
- She stays prone at least 16 hours of every 24 hours, when she can tolerate it.

Why does proning work in ARDS?

- Prone positioning redistributes opacities from dorsal to ventral zones
- If the patient can tolerate, we may see a marked improvement in oxygenation and ventilation
- If no improvement, need to consider more invasive support

Published in: Luciano Gattinoni; Paolo Taccone; Eleonora Carlesso; John J. Marin, Am J Respir Crit Care Med 188 1286-1293.
3 are there any from NEJM or others anyone has come across?  
Michael Lipnick, 9/28/2020

2 There is the NEJM original proning video. We are working on making a video for proning in COVID times :) If USAID wants to throw some $$$  
Lekshmi Santhosh, 10/2/2020

4 what resources do you need?  
what are limitations in existing videos?  
Michael Lipnick, 10/2/2020

1 Here can have picture of proning - just threw this one in with reference:  
https://emcrit.org/pulmcrit/awake-prone-covid/  
Lekshmi Santhosh, 10/2/2020

5 https://www.youtube.com/watch?v=cCkHPYpwg2g  
Michael Lipnick, 10/2/2020

6 Source = https://www.embeds.co.uk/2020/04/08/  
Better if drawn  
Michael Lipnick, 10/2/2020
Oxyhemoglobin Saturation (Spo2) 1 Hour After Initiation of the Prone Position in Awake, Nonintubated Patients With COVID-19

Spo2 before and 1 h after initiation of the prone position in awake, nonintubated patients with COVID-19 severe hypoxic respiratory failure (n = 25).

Figure Legend:

- Proning non-intubated COVID-19 patients may improve oxygenation
- Evidence is limited but promising in non-intubated (“awake”) patients.
- A trial of proning in the setting of escalating oxygen requirements in “awake” patients is low-risk and may be beneficial, but requires close monitoring in case of deterioration.

Case: Key learning points

- COVID-19 pneumonia cases with mild to moderate hypoxemia can be managed with 1-10 L/min
  - 1-6 LPM via NC and 6-10 LPM via facemask (or use both)
  - Humidification should be included for any flow > 6 LPM.
  - A non-rebreather face mask (with bag and reservoir) can increase oxygen delivery to 15 L/min
- Be aware of your facilities oxygen delivery capacity and resources
- Prone positioning may help both oxygenation and ventilation by preventing compression of the lungs and redistributing ventilation and blood flow
- Prone positioning of awake, non-intubated patients may be helpful, is generally quite safe, but requires close monitoring and patient participation
  - but it is unclear if it is specifically helpful in patients with COVID-19

Case #2 (Continued)

- Despite proning and NRB at 15LPM, over the next 12 hours she worsens. SpO2 remains at 88%. Repeat CXR is shown here.
- PI is tachyphneic though appears comfortable without significant accessory muscle use.
- The term ‘happy hypoxemic’ has commonly been used to describe patients with COVID19. While frequently observed, the phenomenon of profound hypoxemia and relative absence of symptoms or increased work of breathing is not a new phenomenon, nor specific to COVID.
Quick Q: Which oxygen delivery device would you select?

1. Nasal Cannula
2. Facemask
3. Venturi Mask
4. Non-rebreather
5. High Flow Nasal Cannula
6. CPAP & NIPPV
7. Ventilator

High pressure high flow delivery devices

- High Flow Nasal Cannula
  - Nasally delivered
  - Can deliver 100% oxygen
  - Requires active heat and humidification to keep airways from drying out
  - Tolerated well and may help avoid mechanical ventilation for a number of COVID patients

- CPAP & NIPPV
  - Delivered by face mask, nasal mask, or helmet
  - 100% oxygen delivery if device accepts high pressure O2
  - Wide range of flow needs (~10-60 liters per minute depending on seal)
  - Delivers pressure in addition to oxygen = more support
  - Limited long-term tolerance (e.g., skin ulcerations)
  - Requires adequate mental status for use

- Ventilator
  - Delivered via a breathing circuit/valved mask in sedated patients, but also can be used to deliver BiPAP or CPAP with a mask
  - Can deliver 100% oxygen
  - Provides higher pressure delivery than CPAP/NIPPV
  - Wide range of flow needs (~15-30 liters per minute depending on patient settings and ventilator type)
  - Tolerated well and may help avoid mechanical ventilation for a number of COVID patients

Audience Response Q

1. NC
2. Face Mask
3. Ventilator
4. Non-rebreather
5. HFNC
6. CPAP & NIPPV
7. Ventilator

Case: Key Learning Points

- Stepwise approach to increasing oxygen therapy
  - Unless the patient requires immediate intubation
  - HFNC may be effective in COVID-19 for treatment of hypoxemia
    - It can use a lot of oxygen
    - May increase aerosolization - N95 for provider, surgical mask for patient!
  - NIPPV is controversial in COVID-19
    - Unclear if helpful in hypoxemia due to COVID-19
    - May increase aerosolization and HCW risk
  - HFNC and NIPPV require close monitoring for deterioration
    - Don’t delay intubation if the patient needs intubation!
Initial management of the hypoxic COVID-19 patient

- Does the patient need intubation?
  - No
    - Choose available oxygen delivery device to keep SpO2 at goal (>88%)
    - Low flow nasal cannula (<6 LPM)
    - Facemask (<10 LPM)
    - Wean to SpO2 > 88-95%

  - Yes
    - Consider Invasive Mechanical Ventilation
      - Use Lung Protective Ventilation Strategy

On frequent evaluation (~q2h), is the patient meeting treatment goals:
- SpO2 (>88%), improving work of breathing, pH>7.30, PaCO2<45, adequate mental status?

If your therapy has not resulted in patient improvement in the above parameters, consider alternative therapies

Choose ~1-2 hour trial of High flow nasal cannula (30-60 LPM) or if unavailable then Non-rebreather (10-15 LPM) or if unavailable then CPAP or if COPD or CHF contribution to respiratory failure, then NIPPV/BiPAP (∆6-10/10-15 PEEP)

YES (continue therapy and re-evaluations)

NO

Caution: Systematic approach to patient evaluation and management of COVID-19 related respiratory failure is essential to optimize outcomes and minimize the impact of respiratory failure.

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The Case

- CC: Shortness of breath, diarrhea
HPI

- 32 year old man with no real PMHx comes to ED for 1 week of diarrhea, abdominal pain, cough and shortness of breath
- PMHx & PSHx: None
- SHx: Never-smoker, rare alcohol, +MJ *
- FHx: None

Physical Exam

VS: T 37, HR 110, BP 100/63, RR 28, O2 83% RA

General: Ill-appearing, diaphoretic, tachypneic

HEENT: Mucus membranes moist, OP clear

CV: RRR, no murmurs/rubs/gallops

Lungs: Bilateral coarse crackles, tachypnea

Abdomen: Benign, +BS, no rebound/guarding

Ext: No clubbing, cyanosis

Imaging

Could this be VAPI?

Vapi

City in India

Vapi, a city and municipality in Valsad District in the state of Gujarat. It is situated near the banks of the Damanganga River, around 20 km south of the district headquarters in the city of Valsad. It is surrounded by the Union Territory of Daman to the west and Dadra and Nagar Haveli to the west. Wikipedia

Weather: 80°F (27°C), wind: 5 mph (8 km/h), 67% humidity
Could this be VAPI?

Vaping Associated Pulmonary Illness (VAPI)

As of September 2019, the Centers for Disease Control (CDC) has reported over 320 cases of vaping associated pulmonary illness (VAPI) across 35 states. The observed patterns of disease are variable but all have been associated with recent electronic cigarette use or "vaping". "Vaping" is a word used to describe the use of an electronic system to deliver inhaled drugs, most commonly nicotine and cannabidiol (natural or synthetic forms of marijuana). "Vaping" is another term that is used to describe the use of a specific vape device.

Your Differential Diagnosis? BESIDES VAPI?

- Type in the ChatBox!

Your Differential Diagnosis? BESIDES VAPI?

Rapidly Progressive Respiratory Failure

- ARDS (Acute Respiratory Distress Syndrome)
- Acute infection – viral +/- bacterial pneumonia
- Massive aspiration
- Acute eosinophilic pneumonia
- Lipoid pneumonia
- (Pulmonary embolism)

Clinical Course

- His hypoxemia worsens and he develops worsened hypoxic respiratory failure requiring intubation
- Now how do you manage him?
**Management Pearls for VAPI**

- Supportive care
- Limited role for steroids
- Bronchoscopy to rule-out infection
- Lung-protective ventilation strategy
- Fluid-conservative strategy
- Report to CDC, SFDPH, and local research teams

**Summary: Key Learning Points**

1. Think of VAPI in people who have vaped within 90 days who have respiratory failure
2. GI sx are common & often people don’t disclose immediately
3. Treat with supportive care & report to CDC and SFDPH & local research teams

**Pulmonary Advocacy re: VAPI**

- **Action Steps**
  - Report all suspected cases to CDC.
  - Screen all patients for the use of tobacco and vaping devices.
  - Offer smoking and vaping cessation counselling to all patients who report use.
  - Support legislation to prevent the sale of vaping and tobacco products to anyone under the age of 21.
  - Support stronger penalties for retailers who illegally sell tobacco, nicotine, and vaping devices to minors.
  - Encourage the FDA and Congress to ban flavors in tobacco products.
  - Support research on prevention and cessation strategies for smoking and vaping.

**Choose Your Own Adventure! Top 6 Cases**

- **Could this be VAPI?**
- **GI Still Queasy**
- **Effusing Confusion**

| A Tickle In the Throat | An International Enigma | Potatoes, Pot-ah-toes |
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It’s Not Easy Being Wheezy

A 55 year old man who has a history of COPD, OSA, CAD, CKD, jaundice, & childhood asthma admitted for dyspnea. He is still wheezing & hypoxemic despite 5 d steroids & antibiotics.

What is your differential diagnosis for his wheezing? Type in the chat box!

ACOS (Asthma-COPD Overlap Syndrome)

All that Wheezes is not Asthma or COPD

- Vocal cord dysfunction
- Allergic bronchopulmonary aspergillosis
- Vasculitides such as Eosinophilic Granulomatosis with Polyangiitis
- Infections such as Strongyloides
- Malignancy (lung or mets)

- Pulmonary embolism
- Decompensated CHF
- Obesity
- Bronchiectasis
- Occupational lung diseases
- Interstitial lung diseases
What About Reactive Airways Disease?

**Pulmonary Perspective**

“Reactive Airways Disease”
A Lazy Term of Uncertain Meaning That Should Be Abandoned

- Different from Reactive Airways Dysfunction Syndrome -
- Acute wheezing in response to inhaled irritant

Diagnostically, When to C/S Pulm?

- Basic diagnostics are not helpful (PFTs, Chest CT)
- You need advanced testing (e.g. methacholine/bronchoprovocation testing, exercise testing, bronchoscopy, etc.)
- You suspect an asthma/COPD mimic
- You just need extra diagnostic help!

Therapeutically, When to C/S Pulm?

- Severe asthma requiring ICU stay - ICU Admission for asthma and intubation are strong predictors for fatal or near-fatal asthma!
- Uncontrolled asthma despite step-up therapy
- You are considering omalizumab or other IgE-mediated tx

Audience Response Q

- What is the BIGGEST change in asthma guidelines?
  A. Start with PRN albuterol for all mild asthma
  B. Start with ATC albuterol for all mild asthma
  C. Start with PRN LABA/ICS for all mild asthma
  D. Start with ATC LABA/ICS for all mild asthma
  E. No big changes, I didn’t hear anything!
New Data from 2019: START Trial

PRN Symbicort is superior to PRN Albuterol for Prevention of Asthma Exacerbations!

New Data from 2019: SYGMA Trials

PRN Symbicort prolonged time to first severe exacerbation

BIG Change in 2019 GINA Guidelines

“The 2019 GINA strategy report represents the most important change in asthma management in 30 years.

For safety, GINA no longer recommends treatment with SABA alone...

GINA now recommends that all adults with asthma should receive either symptom-driven or daily low-dose ICS-containing controller treatment.”

The Changes in Asthma Management
Summary: Key Learning Points

1. All that wheezes is not asthma/COPD
2. Remember ICU admission for asthma is a predictor for fatal asthma in future
3. BIG change in guidelines this year – no more Albuterol PRN only – consider Symbicort PRN
4. Remember non-pharmacologic management & when to consult Pulmonary

Choose Your Own Adventure! Top 6 Cases

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Effusion Confusion: Audience Response Q!

A 65 year old woman is readmitted for pleural effusion of unknown etiology. Last thoracentesis had negative cytology & cx. You:

a. Repeat the thoracentesis
b. Refer for pleurodesis
c. Refer for pleural biopsy
d. Place a PleurX catheter
Never Forget Your Light’s

1. Fluid/serum protein $\geq 0.5$
2. Fluid/serum LDH $\geq 0.6$
3. LDH $\geq 2/3$ normal serum LDH

Chest Tube/Effusion Troubleshooting

- Never place a chest tube to drain hepatohydrothorax.
- Consider serial drainage + diuretics for recurrent transudates
- If drainage slows but effusion persists:
  - Consider reimaging: loculation? tube position?
  - Consider TPA and DNAase
- If chest pain with chest tube beyond expected:
  - Consider: tube dysfunction/malpositioning?
  - Consider complications like infxn, lung lac, diaphragm injury, reexpansion pulm edema

<table>
<thead>
<tr>
<th>Effusion Size</th>
<th>Bacteriology</th>
<th>Chemistry</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal, free-flowing (&lt;10mm)</td>
<td>Neg cv/Gram stain</td>
<td></td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Small-to-moderate free-flowing (&gt;10 mm, but &lt; 1/3 hemithorax)</td>
<td>Neg cv/Gram stain</td>
<td>pH $\geq 7.2$</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Large, free-flowing, 1/2 hemithorax, loculated effusion w/ thickened parietal pleura</td>
<td>Pos cv/Gram stain or frank pus</td>
<td>pH $&lt; 7.2$</td>
<td>Chest tube drainage</td>
</tr>
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2018 ATS Guidelines on MPEs
Summary: Key Learning Points

1. Tap, tap & retap to increase cyto yield
2. Avoid tapping a hepatic hydrothorax
3. For MPE, let prognosis be your guide for next step in management
4. Remember your chest tube troubleshooting tips

Choose Your Own Adventure! Top 6 Cases

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A Tickle in the Throat

55yoM w/ HIV on and off HAART w/ dyspnea

Dyspnea began on July 4th while walking around

Presented to ED & given albuterol nebs → sx resolved → D/Ced from ED w/ albuterol inhaler

Had been using inhaler once/day → q5 minutes

+Wheezing & sensation of tickle in throat

The Consult Question

New C/S: Bronch to r/o PCP. Thx.

History of Present Illness

- Reports no cough, hemoptysis, fevers/chills/sweats
- No myalgias and no sick contacts
- No chest pain/palpitations/PND/orthopnea/lower extremity edema
- No recent travel
- ...Except to his home country of Fiji 2 months ago
To Bronch or Not to Bronch?

Can we? Should we?

A Diagnostic Test Returns....

Type your thoughts in the chat box!
Is Human Immunodeficiency Virus Infection a Risk Factor for *Strongyloides stercoralis* Hyperinfection and Dissemination?

Marc O. Siegel, Larry L. Simon

*Division of Infectious Disease, George Washington University Medical Center, Washington, DC, United States of America*

- **Viewpoints**
  - NOT a traditional risk factor
  - Biggest risk factors are corticosteroid use & HTLV-1
  - Only 40 cases of disseminated Strongy in HIV pts – many were also receiving steroids

- **Diagnosis**
  - Classic sx: GI symptoms (diarrhea), respiratory symptoms (dry cough, throat irritation), skin (itchy red rash when worm enters skin and can get recurrent red rash along thighs & buttocks)
  - Diagnosis usually depends on visualization of the larvae in stool or respiratory culture
  - Stool specimens are very insensitive (<50%)
  - Serology (ELISA) is 83-89% sensitive, 97% specific

- **Management**
  - Treatment is usually ivermectin (200mcg/kg) as first-line treatment, use up to 14 days in case of disseminated strongyloides
  - Can combine with albendazole therapy
  - Monitor w/ repeat stool studies, CBC w/ diff, anti-Strongyloides antibodies
  - Prognosis is good unless you develop bacteremia/sepsis

- **Summary: Key Learning Points**
  1. In HIV patients, travel history is key
  2. Bronchoscopy is the gold standard for diagnosis of PCP ~ 99% yield!
  3. Think of Strongyloides with the triad of eosinophilia, respiratory sx & GI sx
  4. Absence of GGOs on HRCT makes PCP unlikely
Choose Your Own Adventure! Top 6 Cases

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An International Enigma

Chief Complaint

- Abdominal Pain
### History of Present Illness
- 42yo woman visiting SF from Canada
- H/o unilateral lung transplant 16 months ago
- For the last 10 days, has been going to multiple OSH ERs with nausea, vomiting, crampy abdominal pain
- Numerous negative CT Scans

### Past Medical History
- s/p single lung transplant for NSIP
- GERD
- Obesity

### Medications
- CellCept
- Tacrolimus (Prograf)
- PPI
- Septra ppx
- Calcium/Vitamin D

### Physical Exam
- VS: 37.2, HR 79, 132/86, RR 18, 93% RA
- General: Cushingoid appearing woman lying down, appearing fatigued, no acute distress
- Lungs: Fine crackles throughout R lung field, L lung with basilar crackles, no wheezes
- Abdomen: Hypoactive bowel sounds, tender to palpation in mid-epigastrium and RUQ but no rebound/guarding/peritoneal signs, no CVA tenderness, no suprapubic tenderness, no Murphy's signs
OSH Results

- Normal CBC
- Normal CHEM
- Normal LFTs
- Normal CT Abdomen/Pelvis

A Diagnostic Test Returned....

- Tacrolimus level of 21.2!

Tacrolimus Toxicity

- Common sx: fatigue, anorexia, malaise, abdominal pain
- Labs: AKI, hyperkalemia, metabolic acidosis
- Beware of interactions with other drugs!
- Chronic >> acute, especially in renal patients
Summary: Key Learning Points

1. When in doubt, call Transplant team!

1. In any transplant patient, think of:
   a. Infection
   b. Rejection
   c. Recurrence of underlying disease
   d. Medication effect
   e. Post-transplant lymphoproliferative dz

Choose Your Own Adventure! Top 6 Cases

<table>
<thead>
<tr>
<th>Could this be VAPI?</th>
<th>It’s not Easy Being Wheezy</th>
<th>Effusion Confusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Tickle In the Throat</td>
<td>An International Enigma</td>
<td>Potatoes, Pot-ah-toes</td>
</tr>
</tbody>
</table>

Choose Your Own Adventure: Let’s Vote!

A. Could this be VAPI?
B. It’s not Easy Being Wheezy
C. Effusion Confusion
D. A Tickle to the Throat
E. An International Enigma
F. Potatoes, Pot-ah-toes
G. And of course the COVID-19 Case!
Chief Complaint
- Shortness of breath

History of Present Illness
- 73yoM with multiple myeloma s/p chemo (cyclophosphamide, bortezomib, dexamethasone)
- Was admitted with pneumonia a week ago but since discharge still feeling poorly and requiring 6 L NC on readmission
- +Dry cough, no fevers/chills/LEE/orthopnea/PND

Past Medical History
- Multiple myeloma s/p chemo & radiation to ribs
- Meds: Amlodipine, Lexapro, PPI
- Never-smoker, no alcohol, drugs
- No family history

Physical Exam
- VS 37, HR 83, BP 119/69, RR 20, 93% 6 L NC
- Gen: Lying in bed in NAD
- Lungs: RLL and RML crackles, no wheezes, no increased work of breathing
- CV: RRR no murmurs, no JVD
- Ext: No edema
Labs

- Normal CBC & CHEM
- Lower Extremity DVT U/S: No DVT
- Blood cultures negative, Rapid flu negative
- Sputum culture negative

Chest CT Scan

To Bronch or Not to Bronch?

Can we?  Should we?

Bronchoscopy

- Bronchoscopy showed no e/o bacterial, fungal, viral infection and cytology showed no PCP
- So we decided to treat and this happened ...
Latest CXR – Cured!

What was the Diagnosis?

**Radiation Pneumonitis!**

Radiation Pneumonitis/OP 2/2 XRT

- Acute phase usually 4-12 weeks after XRT
- Sx: cough, dyspnea, low-grade fever, chest pain
- Immune-mediated change in capillary permeability
- Classically you see well-demarcated imaging findings
- Treatment is high-dose steroids (1mg/kg) for loooong

Summary: Key Learning Points

1. Always ask re: timing of XRT
2. Check drugs on [www.pneumotox.com](http://www.pneumotox.com) – ESPECIALLY PD1-inhibitors
3. Have to r/o infection before high-dose steroids (& don’t forget PJP prophylaxis!)
### Choose Your Own Adventure! Top 6 Cases

<table>
<thead>
<tr>
<th>Title</th>
<th>Case Study</th>
</tr>
</thead>
<tbody>
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<td>Could This be VAPI?</td>
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### Thank You!
- Lekshmi.Santhosh@ucsf.edu
- @LekshmiMD
Common Inpatient ID Consults

Management of the Hospitalized Patient
October 21, 2021

Jennifer Babik, MD, PhD
Associate Clinical Professor
Division of Infectious Diseases
University of California, San Francisco

Disclosures

- I have no disclosures.

Learning Objectives

At the end of this talk, you will be able to:

- Describe the situations in which formal in-person consultation is preferred over curbside consultation
- Outline an approach to common ID questions that arise in the inpatient setting

Outline

- Curbsides vs Formal Consults
- Top ID Consults
  - Staph aureus bacteremia
  - Blood culture contaminant vs real
  - GNR bacteremia treatment
  - Asymptomatic bacteriuria vs UTI
  - Indeterminate Quantiferon
Outline

- Curbsides vs Formal Consults
  - Top ID Consults
  - Staph aureus bacteremia
  - Blood culture contaminant vs real
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  - Asymptomatic bacteriuria vs UTI
  - Indeterminate Quantiferon

Curbside #1

What is the dose of ertapenem when the CrCl is <30?

Curbside #2

Is This An Appropriate Curbside?

1. Yes
2. No
Is This An Appropriate Curbside?

1. Yes
2. No

Curbside #3

Patient with hx of kidney transplant in 1998 on immunosuppressants, now with diffuse skin rash and fever and new-onset coagulation. Considering leukoerythroblastosis. Should we be concerned about infection from the rash? Is anemia due to infection or GFR? Other patient druggable for prophylaxis?

Curbside #4

I have a theoretical patient with mild cystitis due to VRE that is only sensitive to doxycycline. Does doxycycline penetrate into the urine?
Is This An Appropriate Curbside?

1. Yes
2. No

Are Curbsides Okay?

- Formal consult is preferred in general, but need to balance patient safety, provider workload, education
- Curbside volume in ID is high
- Use e-consults when possible
- Impossible in many practices to convert all inpatient curbsides into formal consults

What is an Appropriate Curbside?

- The Goldilocks of Curbside Consultation
  - Not too simple: can be easily looked up
  - Not too complicated: requires nuanced clinical judgment, data interpretation, reading the literature
  - Just right: Hypothetical, factual question
- We also tell our ID fellows it should be a consult if:
  - You need to look up the answer
  - It's early in the year
  - The team calls you back several times
  - The patient's history is complicated
  - Calls from the ED

Curbsides vs Formal Consults

- Study of 47 curbsides vs. formal consults
  - Medicine consult
  - Curbside → formal consult by a colleague
  - Curbsided providers could not look in chart
- Formal Consults
  - Changed Rx in 60% (36% “major changes”)• If info was inaccurate, then it changed Rx in 92%
  (45% “major changes”)• Information inaccurate or incomplete in 51%

Outline

- Curbsides vs Formal Consults
  - Top ID Consults
    - Staph aureus bacteremia
    - Blood culture contaminant vs real
    - GNR bacteremia treatment
    - Asymptomatic bacteriuria vs UTI
    - Indeterminate Quantiferon

Case #1

60 year old man with lung cancer undergoing chemo admitted with a PICC line infection due to MRSA c/b bacteremia and psoas abscess. PICC line is removed. Cultures only clear after the psoas abscess is drained (positive for 4 days). TEE is negative.

How Long Should He Be Treated With Vancomycin?

1. 2 weeks
2. 3 weeks
3. 4 weeks
4. 6 weeks

ID Consults and Staph aureus Bacteremia

- Benefits of ID consultation (vs no consult):
  -  detection of metastatic foci of infection, endocarditis
  -  removal of prosthetic devices
  -  Improved antibiotic choice and duration
  -  risk of relapse
  -  mortality (by ~20-30%)

- All patients with SAB should have an ID Consult if possible

Curbsides for *Staph aureus* Bacteremia?

- Curbside consult is associated with:
  - Less identification of deep infectious foci (and fewer radiologic tests ordered)
  - Longer duration of fever
  - Less likely to receive the proper duration of therapy
  - Mortality by >2-fold compared to bedside consult

- No curbsides for Staph bacteremia!


My Approach to *Staph aureus* Bacteremia

1. Look for metastatic foci of infection → source control
   - Exam: Brain, lungs, spleen/liver/kidneys, spine, skin, MSK
   - Low threshold for imaging
2. Get surveillance blood cultures
3. Evaluate for endocarditis (TTE vs TEE)
4. Decide appropriate ABx choice
   - Always IV
   - Beta-lactam for MSSA
5. Decide appropriate ABx duration (complicated vs uncomplicated bacteremia)

Antibiotic Choice

- **MSSA**
  - Cefazolin
  - Nafcillin (if need CNS penetration)
  - “Inoculum effect” of cefazolin likely not clinically significant

- **MRSA**
  - Vancomycin
  - Daptomycin
  - If need CNS penetration consider adding rifampin or adding/switching to linezolid

Antibiotic Duration

<table>
<thead>
<tr>
<th>Uncomplicated Bacteremia</th>
<th>Complicated Bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No endocarditis</td>
<td>Does not meet criteria for uncomplicated disease</td>
</tr>
<tr>
<td>2. No metastatic foci of infection</td>
<td>Duration = 4-6 weeks</td>
</tr>
<tr>
<td>3. Repeat blood cx neg at 2-4 days</td>
<td></td>
</tr>
<tr>
<td>4. Defervesce in &lt;3 days of ABx</td>
<td></td>
</tr>
<tr>
<td>5. No prostheses (e.g., prosthetic valves, cardiac devices, joints)</td>
<td></td>
</tr>
<tr>
<td>6. No immunocompromise?</td>
<td></td>
</tr>
<tr>
<td><strong>Duration = minimum 2 weeks (this will be uncommon)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Implanted Prostheses and Antibiotic Duration

- Presence of prosthetic implants in SAB → poor outcomes/complications
  - 2-4 fold risk death, stroke, recurrent infection, metastatic foci
  - This is true even if prosthetic material is not the primary infection/source of bacteremia

- Implant prostheses have high rates of being seeded hematogenously during unrelated SAB
  - 20-50% risk of seeding prosthetic heart valves/rings
  - 30% risk of seeding of prosthetic joints, cardiac devices

Echocardiography in SAB

- Purpose of echo:
  - At least 5-15% of patients with SAB have endocarditis
  - Echo serves to rule out endocarditis as an etiology for or subsequent complication of SAB

- Needed for all?
  - Although there is some debate, most experts agree that all patients with Staph aureus bacteremia should undergo echocardiography (start with TTE)

Transesophageal Echocardiography (TEE)

- Important points about TEE:
  - More sensitive for vegetations (85-90% vs 75% for TTE)
  - Better to evaluate prosthetic valves, device leads
  - Better to evaluate for myocardial abscess
  - May be less sensitive for tricuspid lesions
  - Increased cost and risk compared to TTE

- IDSA: TEE is “preferred” because of higher sensitivity

- In practice, TEE is performed in only 15-80% of patients with SAB

What about TTE in “Low Risk” SAB?

- TTE may have good NPV in a subset of patients with low risk for endocarditis (low quality evidence, somewhat controversial)

- Some experts define low risk as meeting all of the following:
  - Nosocomial-acquired bacteremia
  - Negative blood cultures within 4 days after initial set
  - Absence of prosthetic valve or cardiac device
  - No hemodialysis
  - No clinical signs of IE or secondary foci of infection
A Real World Approach to Echo in SAB

If initial TTE is negative

Low Risk
- Low risk patient
- Low clinical suspicion
- Alternative source

High Risk
- High risk patient
  - Prosthetic valve, cardiac device, congenital heart disease
  - Prior IE
  - IDU or hemodialysis

Moderate-high clinical suspicion
- Community-acquired bacteremia
- New murmur or new conduction abnormalities
- Multiple metastatic foci, embolic lesions, peripheral stigmata
- Prolonged bacteremia or fever

Get TEE only if:
- Poor quality TTE
- ? suspicion during course

Get TEE

Other TEE Considerations

- May consider deferring TEE in:
  - Patients with significant co-morbidities
  - Patients whose GDC are to avoid invasive procedures
  - Patients getting 6 wks of ABx for another reason (eg osteomyelitis) where:
    - There is no concern for intra-cardiac complications (eg conduction abnormalities)
    - ABx regimen would not change if the patient had endocarditis
  - Important to use clinical judgment
  - If defer TEE and give a short course of ABx, consider getting surveillance cultures after stopping

Take Home Points: Approach to Staph Bacteremia

1. Look for metastatic foci of infection → source control
2. Get surveillance cultures
3. Evaluate for endocarditis
   - TTE in all patients
   - TEE if low quality TTE, high risk patient, moderate to high clinical suspicion
4. Decide appropriate Abx (always IV, beta lactam for MSSA)
5. Decide appropriate ABx duration (define bacteremia as complicated or uncomplicated)

My SAB Checklist

SAB checklist:
[ ] Surveillance blood cultures: ***
[ ] Echo: ***
[ ] Original source: ***
[ ] Possible sites of metastatic infection: ***
[ ] Antibiotic choice: ***
[ ] Antibiotic duration: ***
Case #2

Do I need to worry about Bacillus if it grew in the blood? The patient is totally fine and this grew out at 3 days, right after discharge.

Do you need to worry about the Bacillus?
1. Yes
2. No
3. Not sure

How to Determine a Contaminant vs True Infection

- What is the clinical situation?
- What is the organism? Most common contaminants:
  - Coagulase-negative Staph (82%)
  - Corynebacterium (not jeikieum) (>88%)
  - Bacillus spp. (not anthracis) (>92%)
  - Propionibacterium acnes (>94%)
  - Viridans group streptococci (50-55%)
- How many blood culture sets are positive?
  - More likely real if 2 out of 2 sets
  - Caveats: 2/2 common for coag-neg Staph. Check species or antibiograms (100% sensitive for same strain, 84% specific)
- When did it turn positive?
  - Growth at ≥3-5d → more likely contaminant
- # blood culture bottles positive in a set does NOT correlate


Case #3

55 year old woman with MS and h/o neurogenic bladder is admitted with sepsis.

Her urine and blood cultures are growing pansensitive Klebsiella pneumoniae.

She is currently on ceftriaxone and doing well.
How Long Should She Be Treated?
1. 5 days
2. 7 days
3. 10 days
4. 14 days

What Would You Send Her Home On?
1. PO TMP-SMX
2. PO Ciprofloxacin
3. PO Cephalexin
4. IV Ceftriaxone

GNR Bacteremia: Major Questions
- How long to treat?
  - 2 major RCTs on duration of Rx in GNR bacteremia
- Are oral Abx ok?
  - Which ones?
  - 1 large retrospective study and 1 meta-analysis

No further information available on this page.
In General, Shorter is Usually Better!

RCT #1 on Duration for GNR Bacteremia

<table>
<thead>
<tr>
<th>Study #1</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Patient Characteristics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yahav et al, CID 2019 RCT #1 on Duration for GNR Bacteremia</td>
<td>Afebrile, Stable by day 5</td>
<td>Source control</td>
<td>Microbiology: Enterobacteriaceae (62%)</td>
<td>No difference in composite outcome of all-cause mortality, clinical failure, re-admission, LOS&gt;14d (at 90 days)</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>Hereditary, HIV, HSCT, neutropenia (note in the study 25% were ICH and 8% SOT)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Complicated infection: Endocarditis, NSTI, Osteo, CNS, empyema</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Persistent bacteremia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Polymicrobial infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Nonfermenters</td>
<td></td>
</tr>
</tbody>
</table>

RCT #2 on Duration for GNR Bacteremia

<table>
<thead>
<tr>
<th>Study #2</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Patient Characteristics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Dach et al, JAMA 2020 RCT of CRP guided transition (570 vs 306 vs 346 vs 504)</td>
<td>Afebrile x 24h, Stable by day 5</td>
<td>Severe immunocompromised: HIV (69-84; 98% were CRP and CRP&lt;150)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterobacteriaceae</td>
<td>No difference in clinical failure at day 30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urinary, GI source</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Have source control</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinically stable by day 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GNR Bacteremia: Back to Our Questions

How long to treat?

RCT data supports 7 day course of antibiotics for:
- Enterobacteriaceae bacteremia
- Urinary, GI source
- Have source control
- Clinically stable by day 5

Unanswered questions:
- Non-urinary/GI source? (yes)
- ESBL? (yes)
- Immunosuppression? (yes, if not severe)
- When can you switch to orals? Can you use an oral beta-lactam?
GNR Bacteremia: Major Questions

- How long to treat?
  - 2 major RCTs on duration of Rx in GNR bacteremia
- Are oral Abx ok? Which ones?
  - 1 large retrospective study and 1 meta-analysis

Studies of Oral Step Down Rx for GNR Bacteremia

- Tamma et al, JAMA IM 2019
  - Retrospective (n=1478)
  - Inclusion:
    - Enterobacteriaceae bacteremia
    - Stable, could take PO, had source control
  - Exclusion: complicated infections (e.g. osteo)
  - Compared oral step down (got 3d IV then PO) vs all IV for total 14 days
  - Source: GU 40%, GI/biliary 34%, line 18%
  - Results:
    - No diff in mortality, oral group had  LOS
    - Oral group: 70% FQ, 13% TMP-SMX, 17% oral BL
  - No diff between FQ/TMP-SMX vs oral BL

- Punjabi et al, OFID 2019
  - Meta-analysis (8 studies, n=2289)
  - Compared FQ/TMP-SMX vs oral BL for stepdown after 3-5 days of IV therapy (total 14-16 days)
  - 65% FQ, 8% TMP-SMX, 27% oral BL
  - Results:
    - No difference in mortality between oral beta-lactams vs FQ/TMP-SMX
    - Recurrence of infection was more common (OR 2.05) in the oral BL group

What about for ESBL?

- 10-20% of patients in the 7 vs 14 day RCTs had ESBL
- Two additional (small) retrospective studies show that FQ or TMP-SMX are effective as step-down therapy for ESBL bacteremia
- IDSA Guidelines on Treatment of Antimicrobial Resistant Gram Negative Infections: oral therapy with FQ or TMP-SMX is a viable option if otherwise meet clinical milestones for oral therapy

- IDSA Guidelines on Treatment of Antimicrobial Resistant Gram Negative Infections: oral therapy with FQ or TMP-SMX is a viable option if otherwise meet clinical milestones for oral therapy

Are oral Abx ok?

- Oral step-down therapy (by day 3) is safe and effective in:
  - Enterobacteriaceae bacteremia
  - From urinary, GI, lines
  - Source control and clinically stable
  - Especially with FQ or TMP-SMX but likely also oral beta-lactams

Lo et al, JMM 2017, Meije et al, IJAA 2019, Tamma et al, IDSA 2020
### GNR Bacteremia Summary

**Inclusion:**
- Controlled source of infection
- Active IV therapy for at least 48 hours
- Clinically stable, no pressors x 48h
- AF x 48h without anti-pyretics
- Able to tolerate/absorb oral meds
- Organism is susceptible
- Enterobacteriaceae

**Exclusion:**
- Severe immunocompromise
- SOT in last 3 mo or augmented IS
- Neutropenia, HSCT <12 mo, active GVHD
- Complicated infections
- Endocarditis, CNS infection, empyema
- Undraining abscess or infected prosthesis
- Complex urinary anatomy or prostatitis
- Polymicrobial infection
- Persistent bacteremia

### An Approach to Oral Options

<table>
<thead>
<tr>
<th>Tier</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st tier</td>
<td>Ciprofloxacin or levofloxacin (750mg dosing)</td>
</tr>
<tr>
<td>2nd tier</td>
<td>TMP-SMX 8-10mg/kg/day in 2-3 divided doses</td>
</tr>
<tr>
<td>3rd tier</td>
<td>Cefuroxime 500mg PO bid, Amoxicillin 1gm PO tds, Cephalexin 500mg PO qid, Amoxiclav 875/125 bid</td>
</tr>
</tbody>
</table>

**Notes**
- Assuming normal renal fxn
- Cefuroxime > cefpodoxime > cefalexin for GU penetration
- Consider renal function, side effects (eg QTc), DIDs, A days of IV, clinical situation, immunosuppression
- AmpC = Enterobacter, Citrobacter, Providencia, Morganella, Serratia, Haflu

### Case #4

An 89 year old woman with mild cognitive impairment is admitted after a fall with mild mental status changes and inability to care for herself at home. She has no clear localizing symptoms except pain at the site of her fall.

Afebrile, vitals stable.
WBC 10.0
UA 25-50 WBC/hpf

### Does She Need Antibiotics?

1. Yes
2. No
3. Not sure
She was started on ceftriaxone and improved overnight. PT/OT eval for discharge recs is pending.

Urine culture grows >100K E. coli ESBL (sensitive to amp/sulbactam, cipro, ertapenem)

Case Continued

What Would You Do with Her Antibiotics?

1. Amox/clav
2. Ciprofloxacin
3. Ertapenem
4. No antibiotics

New IDSA GUIDELINES for ASB (2019)

Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America®

Asymptomatic Bacteriuria: Definition

ASB = positive urine culture
AND no signs/symptoms of UTI
irrespective of the presence of pyuria

Caveats:
- Voided specimen or indwelling catheter: ≥10⁵ cfu/mL, straight cath specimen: ≥10⁴ cfu/mL
- For women: need 2 consecutive specimens (since often repeat is negative)
Asymptomatic Bacteriuria is COMMON!

- Seen in up to:
  - 20% of elderly, diabetic, HD patients
  - 50% of patients in long term care facilities
  - 70% of patients with spinal cord injury
  - Acquired at 3-5% per day in patients with short-term catheters
  - ~100% of patients with long-term catheters
- Of positive urine cultures obtained on the wards after hospital admission → ~90% are ASB

Exceptions: Who With ASB Should Be Treated?

- Pregnancy
  - Risk pyelo, premature delivery
- GU procedures w/mucosal bleeding
  - Risk post-procedure bacteremia/sepsis
  - 2019 guidelines: Give 1-2 doses, start 30-60 min before the procedure
- Immunosuppressed patients (2019 guidelines)
  - Renal transplant in the first month
  - High risk neutropenia? (IDSA makes no formal rec for or against, but state GU tract is an infrequent source for bacteremia)

Hazards of ASB Treatment

- Side effects of antibiotics
- Risk of C.diff
- Risk of resistance
- May increase risk of recurrent UTI by getting rid of "good" interfering bacteria
- Increased LOS

The Heart of the Problem

- It’s Hard to Ignore a Positive Culture

Proof of concept study:

- At Mount Sinai, 90% of their inpatient urine cultures were ASB, and 50% were treated with ABx
- They stopped reporting these (+) urine cultures in the EMR
- Results:
  - The % of ASB that was treated dropped by 80%
  - No untreated UTIs and no sepsis
How To Distinguish ASB vs. UTI?

- Does the UA help? → Yes, but only if negative
  - Pyuria is seen in >50% of catheterized patients with ASB
  - But the absence of pyuria suggests an alternative dx

- Does the organism help? → NO
  - The same organisms cause ASB and UTI

- Use clinical context – does the patient have signs/symptoms of UTI?


What if I Can’t Assess Symptoms?

How to define UTI in patients with a catheter?

Surrogate signs/symptoms of UTI
- Fever, rigors, malaise
- Flank pain, CVAT, pelvic pain
- Acute hematuria
- Spinal cord injury: spasticity, autonomic dysreflexia, unease

AND No other source of infection (i.e., diagnosis of exclusion)


Interpreting Urine Studies in a Patient With a Foley

- Fever, WBC, etc. → Alternate Diagnosis Likely? (Signs/ sx of other illness present)
  - Yes → Do not order UA, urine cx
  - No → Send UA, urine cx

- UA (-) urine cx (-) → Asymptomatic bacteriuria
- UA (-) urine cx (+) → No
- UA (+) urine cx (+) → Treat for UTI if no alternate dx
- UA (+) urine cx (-) → Do not treat

No other source of infection (i.e., diagnosis of exclusion)

Why?
- Current data does not show causality between bacteriuria and MS changes, and treatment does not improve clinical outcomes
- Places high value on avoiding adverse effects of Abx (Cdiff, resistance)

**ASB vs UTI: Take-Home Points**

- For elderly patients admitted with bacteriuria and AMS, look for other causes and closely observe without antibiotics.
- ASB is very common and rarely needs treatment.
- Pyuria ≠ UTI, but its absence suggests an alternative dx.
- UTI diagnosis in a patient with a catheter requires surrogate signs/symptoms of UTI and no other source of infection.

**Case #5**

23 y/o woman with Takayasu arteritis on prednisone who needs escalation of immunosuppression to infliximab. She has had an indeterminate QuantiFERON (QFT) x 2, negative PPD, and no lung pathology on chest CT. She was born in California and has no known TB exposures or other risk factors. Should she be treated for latent TB infection (LTBI)?

**An Indeterminate QFT Means:**

1. Intermediate probability of LTBI
2. Borderline/equivocal result
3. Low level positive result
4. The test didn’t work

**QuantiFERON Interferon Gamma Release Assay (IGRA)**

1. Nil tube: Negative control
2. TB antigen tube:
   - ESAT-6 + CFP-10
   - Not in BCG or most NTM
3. Mitogen tube: Positive control

Measure IFN-γ by ELISA

Test Readout:
- Positive
- Negative
- Indeterminate
Definition of an Indeterminate Assay

Indeterminate = TEST FAILURE

Positive control (mitogen) didn’t work
(>85% of indeterminate results)

Negative control (nil) had too much background IFN-γ

Reasons for an Indeterminate QFT

<table>
<thead>
<tr>
<th>Test Factors</th>
<th>Patient Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Volume of blood drawn</td>
<td>• Immunocompromise impairs ability of T cells to produce IFN-γ in response to mitogen</td>
</tr>
<tr>
<td>• Suboptimal handling</td>
<td></td>
</tr>
<tr>
<td>• Delays from blood draw to incubation step</td>
<td></td>
</tr>
</tbody>
</table>

How Common is an Indeterminate QFT?

- HCWs and TB Screening Programs: 1%
- Tertiary care inpatient settings: 20%
- Immunocompromise: 5-60%

![Graph](image)
How to Manage Indeterminate QFT?

- If high risk patient → repeat and/or perform a PPD
- Repeat QFT
  - May eliminate possibility of lab-related factors
  - Many will still be indeterminate (40-70%)
  - Consider waiting until CD4 is higher or immunosuppression is decreased
- In a high risk patient, use epidemiologic risk factors, clinical history, chest imaging

T-SPOT TB Test: This DOES Have a Borderline Result

- Mix blood PBMC and TB antigens
- Check for IFN-γ production by ELISPOT
- Also uses a positive and negative control

Test Readout
- Positive (>8 spots)
- Negative (<4 spots)
- Borderline (5-7 spots)
- Invalid (failure of positive or negative control)

Indeterminate QFT: Take-Home Point

- **Indeterminate QFT = test failure** due to failure of either the positive (most likely) or negative control

Thanks For Your Attention!

- Questions?
Caring for the Hospitalized Patient with Addictions

Marlene Martin
Director, Addiction Care Team, Division of Hospital Medicine, SFGH
Associate Professor of Clinical Medicine, UCSF

25th Annual Management of the Hospitalized Patient CME Course
October 21, 2021

I have nothing to disclose

35 Y man admitted with right upper extremity erythema, pain, and swelling

- Started on empiric treatment for cellulitis
- You are receiving sign out from your overnight colleague when you get paged that he is complaining of diarrhea, abdominal pain, headache, and nausea.
- You evaluate the patient and note he is yawning and that his pupils are dilated. He endorses last using heroin right before admission.

Objectives

- Diagnose substance use disorders (SUD) most commonly encountered by hospitalists
- Initiate evidence-based medication for alcohol and opioid use disorder treatment
- Identify how to link hospitalized patients with SUD to addiction treatment on discharge
Outline

- National Landscape of SUD
- Hospitalized patients with SUD
- Diagnosing SUD
- Medication for opioid and alcohol use disorder treatment
- Care Transitions

Tobacco, Alcohol, and Drugs

- 20.4 million (7.4%) had an alcohol or drug use disorder in the last year
- 26.8 million (8.2% of population) smoke cigarettes daily

COVID-19 and SUD

- More than 400,000 tobacco, 25,000 alcohol, and 30,000 drug-related deaths yearly
- Stimulant related deaths are increasing
  - Cocaine related deaths are increasing
  - Methamphetamine related deaths are occurring independent of opioids
- Alcohol-related deaths also rising
- Increase of unhealthy alcohol use among women, older adults, and ethnic minorities
- More rapid acceleration in last few years most prominently among younger age groups and women

SUD Crisis

SUD is prevalent among hospitalizations

Outline

- National Landscape of SUD
- Hospitalized patients with SUD
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- Medication treatment for OUD and AUD

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SUD Crisis

SUD is prevalent among hospitalizations

Outline

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SUD Crisis

SUD is prevalent among hospitalizations
Why treat SUD in the hospital?

2/3 Patients are Motivated to Reduce Use
Pivotal Touch Point

SUD among hospitalized patients
- More likely to be admitted from the emergency department
- Longer lengths of stay, costlier, higher readmission
- High self-discharge rates
- Lower quartile of income
- Unconnected to care

Outline
- National Landscape of SUD
- Hospitalized patients with SUD
- Diagnosing SUD
- Medication for opioid and alcohol use disorder treatment
- Care Transitions
Diagnosing SUD

Symptoms
- Withdrawal
- Intoxication

Diagnoses
- Skin and soft tissue infections
- Endocarditis, osteomyelitis
- Trauma
- Alcohol withdrawal
- Overdose
- Heart failure exacerbation

Not all who use substances have SUD

35 Y man with cellulitis. He uses heroin 3-4 times daily and has been unable to cut back. He lost his job due to missing work and has distanced himself from his parents due to his use. Does he have OUD?

A) Yes
B) No
C) Need more information

35 Y man with cellulitis. He uses heroin 3-4 times daily and has been unable to cut back. He lost his job due to missing work and has distanced himself from his parents due to his use. Does he have OUD?

A) Yes
B) No
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Outline
- National Landscape of SUD
- Prevalence, demographics, and characteristics of hospitalized patients with SUD
- Diagnosing SUD
- Medication treatment for OUD and AUD
- Care Transitions
35 Y man with cellulitis and OUD. What treatments would you offer?

A) Buprenorphine
B) Methadone
C) Clonidine, diphenhydramine, loperamide, Tylenol
D) Extended-release Naltrexone
E) Need more information

Initiating Buprenorphine

- Withdrawal prior to initiation OR
- Gradual uptitration/microdosing

Medications for OUD

- **Opioids**: full mu agonist heroin, oxycodone, fentanyl
- **Methadone**: full mu agonist
- **Buprenorphine**: partial mu agonist
  - High affinity, ceiling effect
- **Extended-release naltrexone**: Full antagonist, high affinity

<table>
<thead>
<tr>
<th>Treatment retention</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher than buprenorphine</td>
<td>Increased retention of doses (1 mg)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Office visits</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily visits to Opiate Treatment Program (OTP) (methadone clinic)</td>
<td>Daily monthly, can also provide as DOT at OTP</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Who can prescribe at discharge?</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTP</td>
<td>Any provider with Opioid Use Disorder (OUD) Waiver</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initiation</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wean high doses, non-tolerant patients or slow metabolizers</td>
<td>No initiation needed</td>
<td>Withdrawal or gradual uptitration/microdosing</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Withdrawal when starting</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takes time to reach comfort zone</td>
<td>Withdrawal or gradual uptitration/microdosing</td>
<td></td>
</tr>
</tbody>
</table>
In methadone Out of methadone In buprenorphine Out of buprenorphine

All cause mortality per 1000 person years

Decreased Mortality

Source: Sordo et al, BMJ, 2017

Hospital Initiation of Buprenorphine

Received bup in the 6 months after discharge Days in bup over 6 months

% Patients

Source: Liebschutz et al, JAMA Internal Medicine, 2014

Detox Doesn’t Last

Patients reporting relapse (%) Days Post-detoxification

Back to our patient. He wants to start buprenorphine. How would you start it?

A) Low-dose or gradual initiation, “microdosing”
B) 2mg buprenorphine
C) 4mg buprenorphine
D) 8mg buprenorphine
E) Need more information

He wants to start buprenorphine. How would you start it?

- Traditionally
  - At least mild withdrawal prior to initiation (COWS 8-11)
- Recent opioids
  - Wait for mild-moderate withdrawal
  - ~8-12h after short acting and 24-48h after long acting
- Transitioning from methadone or fentanyl or no opioid free period
- Ask for help!
- Low-dose buprenorphine/microdose

Withdrawal Assessment
COWS shortcut: Subjective symptoms AND at least 1 objective withdrawal sign
- Subjective: Nausea, abdominal pain, myalgias, chills
- Objective (at least 1): Restlessness, sweating, rhinorrhea, dilated pupils, watery eyes, tachycardia, yawning, goose bumps, vomiting, diarrhea, tremor

Traditional Buprenorphine Initiation

When COWS ≥8, give 2-8 mg
Reassess in 1 hour, then q4-6 hours thereafter.
  - Max day 1: 16 mg
  - Max day 2: 24 mg
Therapeutic dose 16-24mg/day

Increase dose: craving, withdrawal, pain
Decrease dose: insomnia/mania, sedation
Precipitated withdrawal: more buprenorphine OR short acting full opioid agonist

On full opioid agonists or using fentanyl: low-dose, microdosing method

- Depends on buprenorphine formulations available in hour hospital
- Sublingual films or tabs (cut 2mg films or tabs into quarters)
- Buprenorphine patch (patch protocols on next 2 slides)
- Buccal buprenorphine
- Intravenous buprenorphine

- Example protocol using films or tabs:
  - Day 1: 0.5mg q6h = 2mg total
  - Day 2: 1.0mg q6h = 4mg total
  - Day 3: 2.0mg q6h = 8mg total (start decreasing/ stopping full agonists except if acute pain)
  - Day 4: 12-24 mg

Works well with pill-based OUD and heroin use disorder
As you are ordering buprenorphine via a traditional initiation (since he is in moderate withdrawal after last using heroin yesterday) he asks about methadone. What methadone dose would you start?

A) 5mg  
B) 20mg  
C) 100mg  
D) None, we cannot start methadone in the hospital  
E) Need more information

Yes, we can start methadone in the hospital

(c) This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction, or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.

https://www.deadiversion.usdoj.gov

Methadone

- Days at steady dose
- Peak: 3-4 hours
- Half-life: 24-36 hours
- Steady state: 3-7 days
- Risk of overdose with initiation

Monitor on 60mg daily for 5 days before increasing again by 5-10mg, then hold that dose for 5 days, etc.

Target daily dose 80-120mg
Our patient ultimately chooses buprenorphine and is doing well on 16mg daily. However, he has an abscess and goes to the OR for debridement. How would you treat his pain post procedure?

A) Regional block  
B) Morphine  
C) Tylenol  
D) Adjust buprenorphine dosing/frequency  
E) Stop buprenorphine  
F) All of the above

Medication for OUD management in the perioperative period

<table>
<thead>
<tr>
<th>Medication</th>
<th>Verify dose</th>
<th>Before procedure</th>
<th>After procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Call OTP</td>
<td>Continue full dose</td>
<td>Continue full dose, consider splitting dose in the hospital</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Records, PDMP, pharmacy</td>
<td>Continue full dose</td>
<td>Continue/Increase dose, consider splitting</td>
</tr>
</tbody>
</table>

Managing acute pain in the setting of medications for OUD treatment

<table>
<thead>
<tr>
<th>Pain level</th>
<th>Interventions to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild pain</td>
<td>QPSQ (naltrexone/metadone TID)</td>
</tr>
<tr>
<td>Moderate pain</td>
<td></td>
</tr>
</tbody>
</table>
- Buprenorphine, methadone, suboxone 
- Neuroleptics: haloperidol, TCAs, SNRIs |
| Severe pain  | 
- Regional and local anesthesia 
- Give opioids - remember that you will need higher doses due to tolerance 
- Ketamine |

A week later, you admit a 46-year-old woman with depression for alcohol withdrawal and mild alcohol-related hepatitis. She has no primary care clinician, and this is her first presentation. You diagnose her with AUD using the DSM-5 criteria. What options does she have for alcohol use disorder treatment?

A) Naltrexone  
B) Extended-release naltrexone  
C) Acamprosate  
D) Psychosocial treatment (e.g., residential, mutual help group)  
E) All of the above
**AUD Treatment**

**Psychosocial Treatment**

**Medication Treatment**

7.3% receive any treatment

Only 1.6% receive medication for AUD

**2nd Line AUD Medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Mechanism</th>
<th>Adverse Effects</th>
<th>Contraindications</th>
<th>Over Dose</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disulfiram</td>
<td>250 mg</td>
<td>Neutralizes EtOH</td>
<td>Fatigue, nausea, vomiting, depression, headache</td>
<td>Childs ‐ C, Decompensated cirrhosis</td>
<td>Crash lethal</td>
<td>Evidence not strong</td>
</tr>
</tbody>
</table>

**AUD Medications**

**MAINTAIN ABstinence**

- Naltrexone
- Acamprosate
- Topiramate

**DECREASE USE**

- Gabapentin
- Prazepam
- Ondansetron
- Varenicline

* Not FDA approved
Back to our case

46-year-old woman with depression and moderate AUD. Alcohol withdrawal resolves. Her AST/ALT are both <200 and she does not have cirrhosis. She is not receiving opioids. You discuss medications for AUD and psychosocial treatment options with her. She chooses to start naltrexone because of her strong cravings for alcohol and you initiate before discharge.

Increasing Rates of AUD

<table>
<thead>
<tr>
<th></th>
<th>2011-2012</th>
<th>2012-2013</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td>65.4%</td>
<td>72.7%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Risky Drinking</td>
<td>9.7%</td>
<td>12.5%</td>
<td>20.9%</td>
</tr>
<tr>
<td>AUD</td>
<td>8.5%</td>
<td>12.7%</td>
<td>49.4%</td>
</tr>
</tbody>
</table>

As clinicians, we see patients with AUD for...
Outline

- National Landscape of SUD
- Prevalence, demographics, and characteristics of hospitalized patients with SUD
- Diagnosing SUD
- Medication treatment for OUD and AUD
- Care Transitions

Objectives

- Diagnose substance use disorders (SUD) most commonly encountered by hospitalists
- Initiate evidence-based medication for alcohol and opioid use treatment
- Identify how to link hospitalized patients with SUD to addiction treatment on discharge

Opportunities for you to improve SUD care

- DIAGNOSE SUD
- TREAT SUD
- LINK TO CARE
How you can help today

1. Get your X-waiver now!
2. Prescribe naloxone for overdose prevention including stimulants
3. Assess your patients for SUD and their SUD goals
4. Continue SUD medications during admission

Get your X-Waiver Now!

1. Go to: https://buprenorphine.samhsa.gov/forms/select‐practitioner‐type.php
2. To complete the application:
   - Under training you received, click other and mark "practice guidelines"
   - Date: today
   - City: type "Practice Guidelines"
   - State: Type in your state
   - Select 30 patients

Lead systems change

- Offer medications for addiction treatment to patients with SUD
- Create hospital order set or guideline for new starts
- Partner with stakeholders to link patients to community care
- Disseminate knowledge with colleagues
- Become a SUD champion in your hospital

Reflections

Take 1 minute to write down (or tweet):
One concept or tool that you commit to incorporating to improve your care of patients with SUD now
Thank You!
Questions?

ACT.UCSF.EDU
marlene.martin@ucsf.edu
@MarleneMartinMD

Harm Reduction

- NAR = treatment & HR
- Needle exchange programs
- Review injection practices
- Supervised injection facilities
- Buddy system
- HCV and HIV education, screening, and treatment
- HAV, HBV, & Tdap vaccines
- Naloxone
ICU Management Pearls for the Hospitalist

Lekshmi Santhosh, M.D., M.A.Ed.
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Associate Program Director, UCSF Pulm/CC Fellowship
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Management of the Hospitalized Patient 10.21.2021

Disclosures

I have no conflicts of interest to disclose.

Organizational Structure of Closed ICUs

Organizational Structure of Open ICUs
ICU Management Pearls for the Hospitalist
1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy

ICU Management Pearls for the Hospitalist
1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy
Volume Status: The Holy Grail

Classic debate b/w specialties: hospitalists are often the 'arbiters of truth'

Q: When someone is hypotensive, I:

A. Start vaspressors
B. Fluid resuscitate with NS
C. Fluid resuscitate with Albumin
D. Fluid resuscitate with Plasmalyte/LR
E. POCUS, POCUS, more POCUS
F. Just lower the MAP goal.

---

Resist the "Lacto-Bolo Reflex"!

"Fluids for everyone hypotensive!"
All that is Hypotensive is NOT Sepsis: Sepsis Mimics

More Common:
- Hypovolemic
- Hemorrhagic
- Pulmonary Embolism
- Cardiogenic
- Obstructive/Tamponade

More Rare:
- Anaphylactic Shock
- Adrenal Crisis
- Myxedema Coma
- HLH
- Toxidromes

Reassess Patient at the Bedside – Beyond the EHR

The New 65 Trial Addresses a Perennial Question

LaMontagne et al. JAMA 2020

How to Resuscitate? Some Practical Tips

- If not responsive to fluids & escalating pressors, consider “the septic heart” – TTE

- Caution! Normal EF may actually be low in sepsis w/ vasopressors

- Smaller IVF boluses in CHF, ESRD, peri-intubation (250 ccs at a time) – reassess
New Trial! How Quickly to Resuscitate? 999 Ain’t Bad!

- BaSICS RCT (Zampieri, JAMA 2021)
- 10,520 patients in ICUs – 333ml/hr (slow infusion) vs 999ml/hr (fast infusion) rate
- No mortality difference! Bolus away if you need to!

Don’t forget to D/C IVF long before D/C Home!

Key Point

Volume status is dynamic and difficult to assess: reassess frequently and de-escalate & diurese early.

Q: My 1st line vasopressor of choice for shock is:

A. Norepinephrine (Levophed)
B. Phenylephrine (“Neo”)
C. Dopamine
D. Vasopressin
E. Epinephrine
F. Just lower the MAP goal.
**Vasopressor of Choice**

- "Fill the tank" & check for volume-responsiveness
- CENSER Trial discussed early escalation to vasopressors – will need to be replicated
- Almost no role for Phenylephrine “Neo”

**A Plea to Use Generic Names**

- Norepinephrine “Levo”
- Phenylephrine “Neo”

**Vasopressors → ICU. But What about via PIV?**

Small single-centered studies → small systematic review ~3% complications

<table>
<thead>
<tr>
<th>Principle</th>
<th>Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vein size</td>
<td>&gt; 4 mm, measured by U/S</td>
</tr>
<tr>
<td>Location</td>
<td>Upper extremity (no hand or wrist)</td>
</tr>
<tr>
<td>IV line size</td>
<td>20 g or 18 g</td>
</tr>
<tr>
<td>Assessment</td>
<td>RNs assess q2 hrs per protocol</td>
</tr>
<tr>
<td>Maximum dose/time</td>
<td>Low-dose nonepi &lt; 24 hrs</td>
</tr>
</tbody>
</table>

**Quick Pearl on Mixed Shock: Compartments!**

LV  RV  Pulmonary Vasculature
Pressors are like antibiotics: select the correct drug for the patient’s physiology.

New Recs: 93 Recs in October Surviving Sepsis Guidelines!

Highlights of the New Surviving Sepsis Recs

<table>
<thead>
<tr>
<th>KEEP</th>
<th>STOP</th>
<th>START</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Abx (&lt;1 hr)</td>
<td>Using qSOFA!</td>
<td>Balanced crystalloids</td>
</tr>
<tr>
<td>Norepi as 1st line</td>
<td>Starches/gelatins!</td>
<td>HFNC &gt; NIPPV</td>
</tr>
<tr>
<td>Addressing GOC early</td>
<td>Using Vitamin C!</td>
<td>?Steroids?</td>
</tr>
</tbody>
</table>

ICU Management Pearls for the Hospitalist

1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy
Approach to Massive Resuscitation

What Defines a "Massive Transfusion"?

3 most common definitions:
1. Transfusion of ≥ 10 RBCs within 24 hours
   - This approximates the total blood volume of an adult!
2. Transfusion of ≥ 4 RBCs within 1 hr & anticipating more
3. Replacement of >50% total blood volume by products in 3 hrs

Pham et al, Br J Anesthesia, 2011

Epidemiology of Massive Transfusion

1. Major surgeries (spinal, liver transplant, cardiac cases)
2. Trauma (40% of trauma-related death 2/2 hemorrhage)
3. Obstetric hemorrhage (#1 cause of maternal mortality)
4. Gastrointestinal hemorrhage (variceal bleeding esp)
5. Hematologic malignancy

Pathophysiology of Massive Transfusion

Pham et al, Br J Anesthesia, 2011
Permissive Hypotension

- Conceptually part of damage-control resuscitation
- Minimize bloody vicious triad
- Maintain organ perfusion & avoid rebleed & vasoconstriction
- Caveat: CPP = MAP - ICP

Key Point

For massive resuscitation, permissive hypotension is ok, except for brain & spinal cord injury pts

GI Bleed Trials: A Classic Trial

- Villaneuva et al, NEJM 2013 study

Quick Pearls: Jehovah’s Witnesses

- The Case: 60yo woman, Jehovah’s Witness, admitted with Hb of 4 and hypotension.
- Humans can tolerate severe anemia!
- Consider fluids, FeSO4, EPO as adjunct therapies
- Try to get source control; consider Ethics consultation
Quick Pearls: End-of-Life

- The Case: 96yo woman admitted with aortoenteric fistula and hypotension
- Key Point: Massive transfusion is a bridge
- Knowing when to stop is equally important . . .

Key Point

ICU 1 Pager on Massive Resuscitation

ICU Management Pearls for the Hospitalist

1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy
Q: Not Indicated for Non-Invasive Ventilation?

A. Hypercapnic respiratory failure
B. Cardiogenic pulmonary edema
C. Hypoxemia in a DNR/DNI Yoda
D. Weaning from the ventilator

Non-Invasive Ventilation: When to Use it?

- COPD exacerbation with hypercapnic acidosis
- Cardiogenic pulmonary edema
- Post-extubation respiratory failure

Contraindications to Non-Invasive Ventilation

- Cardiac or respiratory arrest
- Facial or neurological surgery/trauma/deformity
- Inability to protect airway/cooperate
- Inability to clear secretions
- High risk for aspiration
- Goals of care

Flow vs. Pressure: Who Wins?

<table>
<thead>
<tr>
<th>NIV</th>
<th>HFNC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counterbalances auto-PEEP</td>
<td>More comfortable than NIV</td>
</tr>
<tr>
<td>Reduces work of breathing</td>
<td>Higher FiO2 delivery</td>
</tr>
<tr>
<td>Improves lung compliance</td>
<td>Decreased dead space</td>
</tr>
<tr>
<td>Mask can be uncomfortable</td>
<td>Not good for hypercapnia</td>
</tr>
</tbody>
</table>
Key Point

Think carefully about contraindications and to what you are bridging. Continually reassess if they need intubation, whether HFNC or NIV.

ICU Management Pearls for the Hospitalist

1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy
## Indications for Tracheostomy
- Prolonged intubation
- Facilitation of ventilation support/weaning
- Upper airway obstruction
- Inability to intubate
- Adjunct to major HEENT surgery/trauma
- Airway protection (neurologic diseases, TBI)

## Advantages of Tracheostomy Intubation
- Pt comfort/decreases work of breathing
- Better speech, swallowing, mobility
- Easier to suction
- Facilitates weaning/x-fer out of ICU
- Easily done in most settings
- Not surgical (risk, $)

## Disadvantages of Tracheostomy Intubation
- Surgical procedure w/ related risks (incl mediastinitis)
- Possible laryngeal nerve injury
- Possible tracheo-arterial fistula
- Stomal/cuff complications
- Risk of tracheomalacia
- Risk of laryngeal injury
- Trauma to nose/mouth

## For these reasons, tracheostomy when indicated may facilitate weaning from mechanical ventilation \( \rightarrow \) Tracheostomy is not a failure!
Trach management: What about COVID?

- Highly infectious pathogen
- Aerosol generating procedure
- Prolonged ventilation
- Prolonged sedation
- Scarce resources

Trach management: Pathways

On Vent - AC/VC Mode
- Trach Surgery
- Trach & Vent - AC/VC Mode
- Trach & Vent - PSV Mode
- Trach Collar
- Trial (Extubation criteria)
- Cuffless Trach
- Downsize
- Capping Trial
- Decannulation!

LTACHs and Weaning

Weaning at an LTACH can go more quickly than you think!
Trach Emergencies: UCSF OHNS QI

- Always know which box is checked for your patient – is your patient ‘intubate-able from above’ or not?
- When in doubt, call a Code Blue!

Patient Expectations

Think about specific indications/advantages of a trach & remember a trach is not a failure. Know the progression pathway to weaning & set patient/family expectations accordingly.

ICU Management Pearls for the Hospitalist

1. Volume, Pressors & Shock
2. Blood, Sweat & Tears
3. Non-Invasive Ventilation
4. Demystifying Tracheostomy
Thank You!

Questions?

Lekshmi.Santhosh@ucsf.edu
@LekshmiMD
ARS: How many COVID-19 vaccines are currently being rolled out worldwide?

1. Three
2. Five
3. Six
4. Nine
5. Fifteen

<table>
<thead>
<tr>
<th>Category or name</th>
<th>Form of publication for phase 3 data/type of vaccine</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>Peer reviewed publication/ mRNA</td>
<td>Baden NEJM, Feb 4, 2021</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Peer reviewed publication/ mRNA</td>
<td>Polack NEJM, December 31, 2020</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Press release only/ adenosine + DNA</td>
<td>FDA document Feb 24</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Two peer-reviewed publications but ongoing (adenovirus + DNA)</td>
<td>Voysey Lancet, December 8, 2020; Polack NEJM, January 2, 2021</td>
</tr>
<tr>
<td>Sputnik 5</td>
<td>Peer-reviewed publication (DNA plus adenosine)</td>
<td>Leitman Lancet, February 3, 2021</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>Publication (whole inactivated)</td>
<td>Sinopharm, JAMA, May 28, 2021</td>
</tr>
<tr>
<td>Sinovac</td>
<td>Publication (whole inactivated)</td>
<td>Sinovac, JAMA May 28, 2021</td>
</tr>
<tr>
<td>Bharat</td>
<td>Press release (whole inactivated)</td>
<td>Bharat Consort, April 21, 2021</td>
</tr>
</tbody>
</table>

There are actually 9 vaccines out there for COVID-19, three authorized in U.S.

6 vaccine candidates to date involve spike protein and receptor binding domain of SARS-CoV-2 either mRNA or adenoviral-vector DNA vaccines or protein adjuvant itself; 3 inactivated virus
Three types of vaccines involving spike protein

- mRNA vaccines (2)
- Adenoviral vector DNA vaccines (3)
- Spike protein + M-adjuvant vaccine (1)

Three vaccines whole inactivated virions

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Adjuvant</th>
<th>Spike protein</th>
<th>T-cell response</th>
<th>Memory response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>lipid</td>
<td>viral</td>
<td>variable</td>
<td>good</td>
</tr>
<tr>
<td>Moderna</td>
<td>lipid</td>
<td>viral</td>
<td>variable</td>
<td>good</td>
</tr>
<tr>
<td>Novavax</td>
<td>protein</td>
<td>viral</td>
<td>variable</td>
<td>good</td>
</tr>
</tbody>
</table>

Remember immunity - antibodies and cell-mediated

**T cells are the major immune defense against viruses, preserved**

- Memory T cells
  - CD4⁺ T cell
  - CD8⁺ T cell
- CD8⁺ T cell
- Memory B cells

Most vaccine trials measured antibodies and T cell responses

---

**How does functional T-cell response modulate severity of disease?**

- T cell responses modulate the severity of disease
- Strong T cell responses in all of these trials seem to have led to prevention of severe disease
- J&J study shows that those with asymptomatic infection mounted good T cell responses to COVID-19
- If you get re-infected after natural infection or vaccine (at one year), should be mild if mounted good T cell response
- Fun fact: Study from 1918 survivors of influenza pandemic show durable B cell immunity (memory B cells) 90 years later!
Will vaccines work against variants and all against severe disease? Short answer: yes because of T cells

<table>
<thead>
<tr>
<th>Company</th>
<th>Platform</th>
<th>Non-clinical results</th>
<th>F with vaccine (same placebo)</th>
<th>Protection from COVID-19 hospitalization</th>
<th>Efficacy against severe COVID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bharat</td>
<td>Inactivated whole virus</td>
<td>2</td>
<td>11,000 Neutralizing Abs</td>
<td>100%</td>
<td>78%</td>
</tr>
<tr>
<td>Sinovac</td>
<td>Whole inactivated virus</td>
<td>2</td>
<td>13,068 Neutralizing Abs</td>
<td>100%</td>
<td>72.8%</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>Whole inactivated virus</td>
<td>2</td>
<td>13,068 Neutralizing Abs</td>
<td>100%</td>
<td>78.1%</td>
</tr>
</tbody>
</table>

Why T cell response will work against variants? First look at natural infection

- Broad T cell repertoire (100s of T cells across spike protein) after infection. Means viral escape of T cell immunity (from both natural infection and vaccination) unlikely, re-infection if happens mild
Then look at T-cell response to variants after vaccines- still intact

- Looked at SARS-CoV-2-specific CD4+ & CD8+ T cell responses from those with natural infection with non-variant & examined activity against alpha, beta, gamma variants
- T cell reactivity against those variants remained intact if you had natural infection or mRNA vaccination (Pfizer/Moderna)
- Same finding from UCSF paper after vaccines, T cell response intact against alpha, beta variants

Are vaccines waning in effectiveness with delta?
We need to first discuss B versus T cells!
You are 29.2 times more likely to get hospitalized if unvaccinated than vaccinated in time of delta.

ARS: What is the protection against hospitalization from Moderna in the US (with delta):

1. 63%
2. 72%
3. 80%
4. 88%
5. 93%

Memory B cells from vax or infection happily adapt to whatever variant they see.
Why have we seen more symptomatic breakthroughs with delta?

- Could be higher viral load
- **Think more likely waning antibodies with time** (protection in nose
- Increasing duration between doses leads to higher antibodies\(^1\) (e.g. 8-12 weeks done in Canada and UK), less symptomatic breakthroughs in those two countries
- Less re-infection with Moderna than Pfizer\(^2\) (Mayo Clinic study with delta) – Moderna given at 4 weeks, Pfizer at 3 weeks
- Luckily, waning antibodies NORMAL, not a GLITCH and are made anew by memory B cells – that is what they do

\(^1\)https://www.nature.com/articles/d41586-021-01299
\(^2\)https://www.science.org/doi/10.1126/science.abm0829

Data from Canada shows Pfizer works better if extend interval to 7-8 weeks

Myocarditis (although mild/rare) more common with Pfizer q3 weeks (Israel) than longer intervals (usually 8)

So, boosters for everyone or a tiered approach?
Antibodies come down naturally but memory B cells produce more if see virus again. Memory B cells ADAPT their antibodies to cover variants; a booster will code for the same antibodies as ancestral strain.

Boosters approved for:
- Immunocompromised
- >65 years
- 18-64 with medical conditions
- Lots of exposure

- Received an organ transplant and are taking medicine to suppress the immune system
- Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
- Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Active treatment with high-dose corticosteroids or other drugs that may suppress your immune response

6.6 billion doses administered worldwide
- And should we give boosters to immunocompetent?
- Or focus on global vaccine equity instead!

ARS: Of the 6.6 billion doses given out worldwide, what % have been administered in low-income countries?
1. 20%
2. 10.2%
3. 5.8%
4. 2.7%
5. 1.2%

https://www.science.org/doi/10.1126/science.abm0829
https://www.medrxiv.org/content/10.1101/2021.05.28.21258025v1
Do vaccines reduce transmission?
Yes, but with delta less so

<table>
<thead>
<tr>
<th>Setting</th>
<th>Reduction in asymptomatic infections</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare workers in England</td>
<td>85%</td>
<td>Hall L., Lancet, April 11, 2021</td>
</tr>
<tr>
<td>Healthcare workers in Israel</td>
<td>75% and 85%</td>
<td>Park L., Lancet, May 6</td>
</tr>
<tr>
<td>Patients in Singapore Health care system</td>
<td>86.7%</td>
<td>Coronavirus, February 27, 2021</td>
</tr>
<tr>
<td>Ministry of Health (nationwide)</td>
<td>98% (largest study)</td>
<td>March 31, 2021</td>
</tr>
<tr>
<td>Israeli general population (Pfizer)</td>
<td>95%</td>
<td>Dagan E., NEJM, February 24, 2021</td>
</tr>
<tr>
<td>Pre-surgical patients in Mayo Clinic system</td>
<td>98%</td>
<td>Coronavirus, February 20, 2021</td>
</tr>
<tr>
<td>Healthcare workers in Cambridge University hospital</td>
<td>75%</td>
<td>Whitehead J., February 24, 2021</td>
</tr>
<tr>
<td>Frontline responders and residents in UK</td>
<td>95%</td>
<td>Davignon J., March 30, 2021</td>
</tr>
<tr>
<td>US population (18+) with (1,000) exposures</td>
<td>98%</td>
<td>Coronavirus, March 30, 2021</td>
</tr>
<tr>
<td>Long-term care facility (24)</td>
<td>98%</td>
<td>National Med, April 4, 2021</td>
</tr>
<tr>
<td>Nursing homes, U.S. (200 residents)</td>
<td>100%</td>
<td>Coronavirus, April 21 and Money, April 28</td>
</tr>
</tbody>
</table>

PRIOR TO THE DELTA VARIANT

1. IgG antibodies measured in trials found in high levels in nasal mucosa
2. Systemic vaccines induce IgA (mucosal immunoglobulin) and recent study shows mRNA-COVID-19 vaccines induce IgA
3. Monoclonal antibodies hasten viral clearance from airways

6. Challenge experiments with macaques in pre-clinical trials show blocking of viral replication (or no low viral RNA) in BAL and nasal swabs (NarazakiNatureRev, 2020; Guebre-Xabier, Vaccine 2020)

Will vaccines decrease transmission? Biological plausibility (4 main reasons)

1. IgG antibodies measured in trials found in high levels in nasal mucosa
2. Systemic vaccines induce IgA (mucosal immunoglobulin) and recent study shows mRNA-COVID-19 vaccines induce IgA
3. Monoclonal antibodies hasten viral clearance from airways
4. Challenge experiments with macaques in pre-clinical trials show blocking of viral replication (or no/low viral RNA) in BAL and nasal swabs (NarazakiNatureRev, 2020; Guebre-Xabier, Vaccine 2020)

How Provencetown, Mass., stress-tested the coronavirus vaccine with summer partying and delta

- Delta variant likely to transmit from symptomatic breakthroughs but less so – will explain (no evidence from asymptomatic)
- Lots of exposure, lots of mild breakthroughs “stress test” but vaccines held up to their promise - prevented severe disease!

Showed us that
1) Delta variant likely to transmit from symptomatic breakthroughs but less so – will explain (no evidence from asymptomatic)
2) Lots of exposure, lots of mild breakthroughs “stress test” but vaccines held up to their promise - prevented severe disease!

- Delta variant likely to transmit from symptomatic breakthroughs but less so – will explain (no evidence from asymptomatic)
- Lots of exposure, lots of mild breakthroughs “stress test” but vaccines held up to their promise - prevented severe disease!
Delta variant not as infectious in vaccinated as unvaccinated though

- More transmissible
- Likely not as infectious from vaccinated than unvaccinated (Provincetown outbreak data looked at one point in time of CT values of PCR tests in vaccinated & unvaccinated being same)
- Singapore study of delta breakthroughs did serial testing and found viral loads (by CT) drop more quickly among the vaccinated
- NPIs work against delta

Looked at culture data from delta breakthroughs in vaccinated HCWs
Less likely to be infectious by culture data

Bottom line: Vaccinated people can likely spread if symptomatic with delta, but less than unvaccinated

Singapore tracing study showing asymptomatic vax’d spread rare (our post-doc counted 1 transmission from asymptomatic vax’d)

CDC breakthrough data

- CDC keeping track of breakthrough infections in U.S
- Out of >187 million Americans who are fully vaccinated against COVID-19
  - 13.775 hospitalised breakthroughs (0.01%) – 67% >65 years
  - Deaths: 0.003% for COVID-19 (85% >65 years)

https://www.cdc.gov/vaccine/covid-19/health-departments/breakthrough-cases.html
State of the pandemic

USA cases coming down but occurred fastest in states with high rates of vaccination.

California Now Has Nation’s Lowest Virus Transmission Rate

ARS: What are the only two infectious diseases that have been eradicated worldwide?

1. Polio and smallpox
2. Filariasis and smallpox
3. Rinderpest and smallpox
4. Measles and smallpox
5. Filariasis and polio

Features of eradicable infectious diseases – like smallpox

• No animal reservoir
• Clear pathogenic features
• Short period of infectiousness
• Immune for life and then highly effective vaccine

• (COVID-19 looks like other respiratory illnesses, can spread when presymptomatic, in animals, vaccine good)

COVID-19 likely to be controlled not eradicated – so frequency of boosters will depend on if we tamp down transmission WORLDWIDE

- Control: Reducing of disease incidence to acceptable levels
- Elimination: Reduction to zero incidence in a defined geographical area
- Eradication: Permanent reduction to zero worldwide
- Extinction: Infectious agent no longer exists in nature or laboratories.
Pertussis comes under control/elimination with vaccines (measles) and vaccines/treatment (pertussis).

ARS: What is the only outpatient oral treatment for COVID-19 that looks like it works?

1. Hydroxychloroquine
2. Ivermectin
3. Molnupiravir
4. Monoclonal antibodies
5. AZT
PFIZER AND BIONTECH ANNOUNCE POSITIVE TOPLINE RESULTS FROM PIVOTAL TRIAL OF COVID-19 VACCINE IN CHILDREN 5 TO 11 YEARS

September 20, 2021

- Results on file from a pivotal trial of any COVID-19 vaccine in individuals over 12 years of age
- In participants 5 to 11 years of age, the vaccine was safe, well tolerated and showed robust neutralizing antibody responses
- Considers plans to submit these data to the FDA, EMA and other regulatory agencies around the world as soon as possible
- Results in children under 5 years of age are expected as soon as late this year

Summary

- Vaccine trials show amazing efficacy and safety
- All vaccines reduce severe disease significantly, likely due to T-cell response
- Vaccines decrease transmission but more symptomatic and transmission with delta
- Variants can be managed - B cells
- Rare safety concerns – much more rare than COVID itself
- Molnupiravir, child vaccines coming – COVID getting under control
Where did we come from?

Excerpts from an early COVID lecture, 7 March 2020

The state of the Covid-19 pandemic

George W. Rutherford, M.D., A.M.
Professor of Epidemiology, Preventive Medicine, Pediatrics and History
Head, Division of Infectious Disease and Global Epidemiology
Department of Epidemiology and Biostatistics
School of Medicine
University of California, San Francisco

COVID-19 by date of report, China, 18 February-5 March 2020

COVID-19 outside of China by region and week, 20 January to 6 March 2020

*To-date, 6 March
How will this end?

- Containment - increasingly unlikely
  - Keep large bulk of infection in China (currently 89%)
  - But large new clusters in Iran, Italy and South Korea with regional spread
  - New clusters of transmission will require aggressive follow up, isolation and quarantine
  - Spring weather may give us a break
  - Key: rapid response to suspected cases
- Pandemic spread
  - Spread outside of China and sustained person-to-person transmission in other countries
  - Iran, Italy and South Korea
  - U.S. (Washington state, California)
  - How the EU handles COVID-19 will be key
  - Attack rate somewhere between <1% and 20%
  - Potentially very taxing on healthcare system (5% with critical disease)
  - Endemic cause of viral pneumonia?
  - Summer Olympics in Tokyo – what will happen?

Where do we stand?

Worldwide, national, statewide and local epidemiology of COVID-19 and SARS-Co-2
COVID-19 cases per 100,000 by state, last 7 days, United States, October 2021

<table>
<thead>
<tr>
<th>State</th>
<th>Cases per 100,000</th>
<th>7-Day Rate</th>
<th>Risk Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>215,750</td>
<td>7.6</td>
<td>Medium</td>
</tr>
<tr>
<td>Hawaii</td>
<td>269</td>
<td>2.0</td>
<td>Low</td>
</tr>
<tr>
<td>Montana</td>
<td>86</td>
<td>0.4</td>
<td>Very Low</td>
</tr>
<tr>
<td>South Dakota</td>
<td>113</td>
<td>1.0</td>
<td>Medium</td>
</tr>
<tr>
<td>Guam</td>
<td>103</td>
<td>1.0</td>
<td>Medium</td>
</tr>
<tr>
<td>Ohio</td>
<td>8,595</td>
<td>273.0</td>
<td>Very High</td>
</tr>
<tr>
<td>Indiana</td>
<td>1,131</td>
<td>14.9</td>
<td>High</td>
</tr>
<tr>
<td>Kentucky</td>
<td>2,947</td>
<td>83.4</td>
<td>Very High</td>
</tr>
<tr>
<td>Minnesota</td>
<td>2,304</td>
<td>57.7</td>
<td>High</td>
</tr>
<tr>
<td>Oregon</td>
<td>11,789</td>
<td>54.0</td>
<td>High</td>
</tr>
</tbody>
</table>

Risk levels for unvaccinated people

Hospital ICU utilization by catchment area, United States, July-September 2021

COVID-19 mortality rates by county, United States, June 16-October 1, 2021
Statewide indicators, SARS-CoV-2 infection, California, 2021

- $R_t = 0.81$
- 2.6% test positivity
- Hospitalizations 5/292 (14-day change: -21%)

Where are we going?

What can still go wrong?

1. Maldistribution of vaccine with substantial pockets of underimmunization that can sustain epidemic transmission
2. Emergence of more transmissible and less immunologically susceptible variants
3. Loss of confidence in vaccines and more vaccine hesitancy
4. Underutilization of newer technologies
5. Ignoring international spread
Vaccination coverage is highly variable in the U.S. 

COVID-19 death rates by vaccination status, California and United States, 2021

COVID-19 vaccine doses administered, California, 2021

Currently vaccinating
- All Californians ≥12 years old
- Those requiring third doses and booster doses
- 49,028,206 doses administered
- 91,276 average per day for the last 7 days
- 67% of Californians have received ≥1 dose
- 60.4% have been fully vaccinated
- San Francisco: 80.8% with ≥1 dose, 75.9% fully vaccinated

1. Maldistribution of vaccine with substantial pockets of underimmunization that can sustain epidemic transmission
2. Emergence of more transmissible and less immunologically susceptible variants
3. Loss of confidence in vaccines and more vaccine hesitancy
4. Underutilization of newer technologies
5. Ignoring international spread
What is a variant?

• A group of coronaviruses that share the same inherited set of distinctive mutations is called a variant. If enough mutations accumulate in a lineage, the viruses may evolve clear-cut differences in how they function.

• SARS-CoV-2 variants of public health interest are in the spike protein (1,273 amino acids long)

Key mutations present in variants with reduced neutralization are around edge of ACE2 binding site

SARS-CoV-2 variants of concern, United States and California, 2021

Region including: California, Arizona, Hawaii, Nevada and all territories

B.1.617.2 (delta) 98.9%
Delta Plus (delta+) 0.6%
AY.2 0.2%
AY.1 0.4%
B.1.1.7 (alpha) 0.0%
P.1 (gamma) 0.0%
B.1.621 0.0%
Other 0.5%

Rate of change

Covid-19, estimated transmissibility* of variants compared with original SARS-CoV-2 virus

<table>
<thead>
<tr>
<th>Variant (first identified)</th>
<th>Scientific name</th>
<th>Rate of change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta (India)</td>
<td>B.1.617.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Gamma (Brazil)</td>
<td>P.1</td>
<td>1.5</td>
</tr>
<tr>
<td>Alpha (United Kingdom)</td>
<td>B.1.1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>Beta (South Africa)</td>
<td>B.1.351</td>
<td>2.5</td>
</tr>
<tr>
<td>Epsilon (Zimbabwe)</td>
<td>B.1.427-6</td>
<td>3.0</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td></td>
<td>3.5</td>
</tr>
</tbody>
</table>

*Rate of change if factor or relative risk number.
Considerations for future variant emergence

- Lower transmission = less viral replication = fewer opportunities for variants to emerge
- But, as more people are vaccinated, there will be more immune pressure and possible escape
- However, the delta variant seems to be outcompeting other variants suggesting that our worst problem is before us right now
- And the current vaccines work pretty well against delta
- We have redundant immune systems and both cellular (T-cell) and humoral (B-cell, antibodies) immune systems
- Herd immunity is a moving target (waning immunity vs. boosters)
- Lower transmission
- Immunocompromised individuals will be protected by the herd

1. Maldistribution of vaccine with substantial pockets of underimmunization that can sustain epidemic transmission
2. Emergence of more transmissible and less immunologically susceptible variants
3. Loss of confidence in vaccines and more vaccine hesitancy
4. Underutilization of newer technologies
5. Ignoring international spread
Reasons for vaccine failure

• Mishandling
• Immunocompromise
• Therapeutics (e.g., tocilizumab)
• Genetic drift – variants
• Waning immunity

Failure to vaccinate (or to seek vaccination)
COVID-19 cases by vaccination status, Los Angeles County, May-July, 2021


FDA and CDC recommend booster dose for certain Pfizer-BioNTech vaccine recipients

- Newest recommendations
  - All adults ≥15 years old
  - Residents of long-term care facilities
  - People with underlying medical conditions that place them at risk of severe COVID-19
    - 65+ years old can self refer
    - 50–64 years old need to be assessed individually
    - Persons whose occupations put them at risk of exposure
    - Healthcare workers
    - Certain frontline institutional workers
  - Moderna and J&J boosters will be considered on October 14-15

- People with certain medical conditions that place them at higher risk of severe COVID-19 outcomes (50-64 years old should 18-49 may)
  - Cancer
  - Chronic kidney disease*
  - Chronic lung diseases
  - Dementia or other neurologic conditions
  - Diabetes mellitus
  - Down syndrome
  - Heart conditions
  - HIV infection
  - Immunocompromised state*
  - Liver disease
  - Overweight and obesity
  - Pregnancy and recent postpartum
  - Sickle cell disease or thalassemia

- Smoking, current or former
- Solid organ or blood stem cell transplant*
- Stroke or cerebrovascular disease
- Substance use disorders
- People aged 18–64 years at increased risk for COVID-19 exposure and transmission because of occupational or institutional setting
  - First responders (healthcare workers, firefighters, police, congregate care staff)
  - Teachers, support staff, daycare workers
  - Food and agriculture workers
  - Manufacturing workers
  - Corrections workers
  - U.S. Postal Service workers
  - Public transit workers
  - Grocery store workers

*Should receive additional dose regardless of age or primary series
**Status of pediatric COVID-19 vaccines**

- Pfizer announced results today
- Study of >2,000 5-11 year olds
- Comparable neutralizing antibody levels as in previous study of 16-25 year olds (proxy marker)
- Common side effects: pain, fatigue, headaches, chills, mild fever, myalgia for 1-3 days; no cases of myocarditis
- Now goes to FDA for approval of extended EUA (October 26)

---

**SARS-CoV-2 antigen tests**

- Test for the presence of viral proteins rather than viral RNA (which is what PCR tests for)
- Lower sensitivity than PCR but highly sensitive during period of peak infectiousness
- Several are available over the counter or by prescription for home use
- Additionally, two nucleic acid tests have been authorized for home use

<table>
<thead>
<tr>
<th>Name</th>
<th>Manufacturer</th>
<th>How to use</th>
<th>Retail Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>BinaxNOW</td>
<td>Abbott</td>
<td>2-3x with 24-36 hours between tests</td>
<td>$14-24 for two</td>
</tr>
<tr>
<td>Flowflex</td>
<td>ACON</td>
<td>One time</td>
<td>$25 for one test</td>
</tr>
<tr>
<td>Ellume</td>
<td>Ellume</td>
<td>One test</td>
<td>$26-39 for one test</td>
</tr>
<tr>
<td>QuickVue</td>
<td>Quidel</td>
<td>2x with 24-36 hours between tests</td>
<td>$24-25 for two</td>
</tr>
</tbody>
</table>

Other authorized home tests: Becken Dickinson BD (Ventor), Accura Bio (CanclSure), OraSure (InteliSens)

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**Post-exposure prophylaxis with REGEN-COV antibody, household contacts of COVID-19 patients**

One 1200 mg dose of REGENCOV (600 mg each of casirivimab and imdevimab) subcutaneously within 96 hours of household exposure

---

1. Maldistribution of vaccine with substantial pockets of underimmunization that can sustain epidemic transmission
2. Emergence of more transmissible and less immunologically susceptible variants
3. Loss of confidence in vaccines and more vaccine hesitancy
4. Underutilization of newer technologies
5. Ignoring international spread
1. Maldistribution of vaccine with substantial pockets of underimmunization that can sustain epidemic transmission
2. Emergence of more transmissible and less immunologically susceptible variants
3. Loss of confidence in vaccines and more vaccine hesitancy
4. Underutilization of newer technologies
5. Ignoring international spread

What have we learned?
What could we have done differently and how do we respond next time?

U.S. will support compulsory licensing of COVID vaccines
- Waiver of intellectual property for public health emergencies
- WTO allows under TRIPS
- Countries who apply for waiver can manufacture their own vaccines or biologics without IP infringement
Lessons learned for future pandemics

• Early warning systems are key with focus on human-animal interfaces (OneHealth approach)
• Internationalism is essential
• Employ private sector solutions for manufacturing and distributing early prototype diagnostic and screening tests
• Strengthen domestic and global health architecture for pandemic preparedness and response
• Invest in public health and rebuild public health infrastructure

In summary

• As with any vaccine preventable disease, primary reason for incident cases is failure to vaccinate
• Counties with highest incidence have lowest immunity (natural plus vaccine-acquired immunity)
• Breakthroughs remain rare (about 1/3600 fully vaccinated people)
• We seem to be coping with the delta variant (at least in California)
• Likely to continue to see outbreaks in non-immune populations through fall – will we see another winter peak like in 2020-2021?
• What eventually happens in school children will depend on (1) community levels of transmission, (2) 12-to-17-year-old vaccination coverage (currently very high) and (3) how soon mRNA vaccine will be approved for 5-to-11-year-old students (FDA will review on 26 October)
• Potential for influenza A and RSV syndemics
High Yield Neurological Examination

Vanja Douglas, MD
Sara & Evan Williams Foundation Endowed Neurohospitalist Chair
Director, Neurohospitalist Division
Associate Professor of Clinical Neurology
UCSF Department of Neurology

Purpose of Neuro Exam

• Screen asymptomatic patients
• Screen patients with symptoms that could indicate a focal neurologic lesion (e.g. back pain, headache, seizure)
• Localize the lesion in patients with neurologic deficits
  • Generate a differential diagnosis
  • Decide what test to get next (e.g. brain MRI, spine MRI, EMG/NCS, CK)

Typical “Screening” Neuro Exam

• Mental Status: Level of alertness, orientation, attention, language, memory
• Cranial Nerves: I through XII
• Motor: Bulk, tone, power in all muscles in both arms and legs
• Sensory: Light touch, vibration/joint position sense, pain/temperature, Romberg
• Reflexes: Biceps, triceps, brachioradialis, knees, ankles, plantar response
• Coordination: Finger-nose-finger, heel-knee-shin
• Gait: Observe gait, include tandem, heel, and toe walking

Disclosures

None
High Yield Screening Neuro Exam

- Mental Status
- Cranial Nerves
- Motor
- Sensory
- Coordination
- Reflexes
- Gait

Language

<table>
<thead>
<tr>
<th>Expressive Aphasia</th>
<th>Conduction Aphasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluency</td>
<td>Impaired</td>
</tr>
<tr>
<td>Comprehension</td>
<td>Intact</td>
</tr>
<tr>
<td>Repetition</td>
<td>Impaired</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Receptive Aphasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluency</td>
</tr>
<tr>
<td>Comprehension</td>
</tr>
<tr>
<td>Repetition</td>
</tr>
</tbody>
</table>

Extraocular Movements
High Yield Screening Neuro Exam

- Mental Status: language, orientation, and attention
- Cranial Nerves: visual fields, eye movements, and facial symmetry
- Motor
- Sensory
- Coordination
- Reflexes
- Gait

Motor System

2 minute screen for upper motor neuron weakness:

- Pronator Drift
- Finger taps & Foot taps
- Distal extensor power:
  - Finger extensors
  - Tibialis anterior
High Yield Screening Neuro Exam

- Mental Status: language, orientation, and attention
- Cranial Nerves: visual fields, eye movements, and facial symmetry
- Motor: Pronator drift, finger and foot taps, finger extensor and extensor hallucis longus power
- Sensory
- Coordination
- Reflexes: Biceps, knees, and ankles
- Gait

Why Do A Sensory Exam?

- If there are sensory complaints
- If there are balance complaints or a gait disorder
- If there is weakness

Coordination & Gait

- Hemispheres:
  - Finger-nose-finger
  - Heel-knee-shin
- Vermis:
  - Gait
High Yield Screening Neuro Exam

- Mental Status: language, orientation, and attention
- Cranial Nerves: visual fields, eye movements, and facial symmetry
- Motor: Pronator drift, finger and foot taps, finger extensor and extensor hallucis longus power
- Sensory: (If done, do pain OR temp + vibration OR JPS)
- Coordination: Finger-nose-finger and heel-knee-shin (can replace HKS with gait)
- Reflexes: Biceps, knees, and ankles
- Gait: Observe gait (base, stride, posture, arm swing, turn), tandem

Think Like A Neurologist

- Chief Complaint: suspected localization
- History: refine the localization
- Exam: pick maneuvers that rule in or rule out your suspicions

Let’s practice!
Case Scenarios
Patient #1

- A 23 y/o woman with a history of migraine headaches is admitted to the hospital with left leg cellulitis. On hospital day 2, she complains of a new headache. She says it’s different from her previous migraines because it is “much worse” and is wondering if she needs an MRI.

Headache

Suspected localization
- Focal brain lesion

Patient #2

- 57 y/o man hospitalized with MI is altered after his cardiac cath. He is somnolent but arousable, mumbling incoherently. His family is very concerned that he has had a stroke.
Altered Mental Status

**Suspected localization**
- Bilateral hemispheres
- Brainstem

Patient #2 Exam

- Arouses to touch
- Names simple objects, repeats short phrases, follows simple commands
- Disoriented and unable to test attention
- EOMI; face symmetric; blinks to threat bilaterally
- Left arm drifts and hand is clumsy
- Withdraws less briskly to pain in the left leg
- Head CT is normal

Multifocal Strokes

Patient #3

- A 65 y/o man with prostate cancer presents with bilateral leg weakness and urinary urgency.
Bilateral Leg Weakness

Suspected localization
• Spinal cord
• Cauda equina
• Neuropathy
• Neuromuscular junction
• Muscle

<table>
<thead>
<tr>
<th></th>
<th>UMN</th>
<th>LMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern of Weakness</td>
<td>Premonadial</td>
<td>Variable</td>
</tr>
<tr>
<td>Function/Immunity</td>
<td>More alternate motion rate</td>
<td>Impairment of function is mostly due to weakness</td>
</tr>
<tr>
<td>Tone</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Tendon Reflex</td>
<td>Increased</td>
<td>Decreased, absent or normal</td>
</tr>
<tr>
<td>Other signs</td>
<td>Babinski sign, other CNS signs, e.g., aphasia, visual field cut</td>
<td>Atrophy (except with problem of neuromuscular junction)</td>
</tr>
</tbody>
</table>

Spinal Cord Cross-Section

Patient #3: Exam

• Decreased EHL power bilaterally
• Slow foot taps
• Brisk knee jerk and ankle jerk reflexes
• Reduced joint position sense in toes
• Sensory level to pinprick at T5
Metastastic Spinal Cord Compression

Patient #4

- A 30 y/o woman with lupus, APLAS, and history of endocarditis on gentamycin presents with acute vertigo.

Vertigo

- Suspected localization:
  - Brainstem (central)
  - Cerebellum (central)
  - Inner ear (peripheral)

Hypothesis-Driven Neuro Exam
HINTS

- Head Impulse Test
  - Abnormal = peripheral
- Nystagmus
  - Unidirectional = peripheral
  - Direction-changing = central
- Test of Skew
  - Skew deviation = central
- https://youtu.be/1q-VTKPweuk

Patient #4: Exam

- Left beating nystagmus in left-gaze only
- Positive head thrust test to the right

Gentamycin Toxicity

Summary

- High yield screening exam
- Hypothesis driven approach to:
  - Suspected focal brain lesion
  - Altered mental status
  - Suspected spinal cord lesion
  - Vertigo
### Bonus Case

- A 32 y/o woman presents with tingling in the hands and feet that progressed to diffuse weakness in the arms and legs over four days. She is now so weak she can no longer sit up.

### Diffuse Weakness

**Suspected localization**
- High spinal cord
- Neuropathy
- Neuromuscular junction
- Myopathy

---

### Localization of Weakness

<table>
<thead>
<tr>
<th>Pattern of weakness</th>
<th>Tone</th>
<th>Bulk</th>
<th>Reflexes</th>
<th>Sensory Loss</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Motor Neuron</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyramidal</td>
<td>Spastic</td>
<td>Normal</td>
<td>Increased</td>
<td>Varies</td>
<td></td>
</tr>
<tr>
<td>Anterior Horn Cell</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyramidal or myotomal</td>
<td>Spastic or normal</td>
<td>Atrophy</td>
<td>Increased or decreased</td>
<td>None</td>
<td>Fasciculations</td>
</tr>
<tr>
<td>Peripheral Nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In distribution of root or nerve</td>
<td>Normal or reduced</td>
<td>Atrophy</td>
<td>Decreased</td>
<td>Prominent</td>
<td></td>
</tr>
<tr>
<td>Neuro-muscular Junction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal (myasthenia) or Absent (botulism)</td>
<td>None</td>
<td>Phosis and ophthalmoplegia</td>
</tr>
<tr>
<td>Muscle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal &gt; Distal</td>
<td>Normal</td>
<td>Normal or patterned atrophy</td>
<td>Normal</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

### Bonus Case

- Diffuse weakness throughout both arms and legs in both flexors and extensors
- No sensory level
- Decreased pinprick sensation in the feet
- Diffusely absent reflexes
Next Step?

- Lumbar puncture:
  - Protein 143
  - WBC 2
- Guillain-Barre Syndrome

Acknowledgements

- Hooman Kamel
- Andy Josephson
- Dan Lowenstein
- Ann Poncelet
Algorithmic Approach to Lung Opacities

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University of California, San Francisco

Approach to lung opacities

- This is hard!
- You will not be an expert today
- Approach
- Practice
- Think like a pathologist

Categories of lung opacities

- 1. Consolidation
- 2. Interstitial (diffuse lines or nodules)
- 3. Airways
- 4. One or a few nodules
Consolidation

- Confluent opacity
- Fluffy around periphery
- Air bronchograms
- Lack of volume loss

Confluent opacity, no volume loss

Air bronchograms
Consolidation

- Acute vs. chronic symptoms
- Distribution
- Acuity of changes
- Differential diagnosis in acute setting
  - Focal: pneumonia/aspiration, hemorrhage
  - Diffuse: edema, acute lung injury, pneumonia, hemorrhage

Invasive mucinous adenocarcinoma
Chronic alveolar disease

- Tumor
  - Invasive mucinous adenocarcinoma (aka multifocal bronchioalveolar CA)
  - Lymphoma (recurrent or 1° pulmonary)
- Inflammatory
  - Organizing pneumonia
  - Chronic eosinophilic pneumonia
  - Sarcoidosis
- Other
  - Lipoid pneumonia
  - Alveolar proteinosis

Comparison

Signs of atelectasis: volume loss

- Fissure displacement
- Deviation of mediastinal structures
- Elevated diaphragm
Atelectasis (types)

- Obstructive/resorptive (obstruction of bronchus)
- Passive (compression of lungs)
- Cicatricial (related to scarring)
- Adhesive (surfactant deficiency)
Lung cancer (Golden S sign)

Lower lobe atelectasis

Combined RML/RLL atelectasis
Left upper lobe collapse

- Veil-like density
- Volume loss
  - Elevated diaphragm
  - Elevated left PA
- Luftsichel sign

Interstitial opacities

Nodules: diff dx

- Hematogenous spread
  - Miliary tuberculosis
  - Miliary fungal infection (e.g. cocci)
  - Metastases
- Lymphatic spread
  - Sarcoidosis
  - Lymphangitic spread of tumor
  - Pneumoconioses (e.g. silica)
Histoplasmosis

Miliary tuberculosis

Interstitial: lines

Causes of interstitial lines

• Edema
• Malignancy

Kerley-b lines may be present

• Fibrotic lung diseases (this is a long list)

These lines are typically thick, wavy and irregular
Linear opacities

Pulmonary edema (kerley-b lines)
Reticular opacities (distribution)

- Lower lobe predominant
  - Idiopathic pulmonary fibrosis
  - Connective tissue disease
  - Drugs
  - Asbestosis
  - Hypersensitivity pneumonitis
- Upper lobe predominant
  - Sarcoidosis
  - Prior TB/fungus
  - Pneumoconioses

Idiopathic pulmonary fibrosis

Hypersensitivity pneumonitis

Tuberculosis
Airways disease

- Circular

- Tubular
Differential diagnosis of airways disease

- Mild:
  - Asthma
  - Viral infection
  - Chronic bronchitis
  - Etc.

- Severe:
  - Bronchiolitis obliterans
  - Immunodeficiency
  - Ciliary dyskinesia
  - Cystic Fibrosis
  - ABPA
  - Tuberculosis
  - Cartilage diseases

Cystic fibrosis

Which compartment of lung is affected?

- Granuloma
- Hamartoma
- Primary bronchogenic carcinoma
- Metastasis
- Lots of others

Solitary pulmonary nodule: differential diagnosis
### Nodules: benign vs. malignant

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small size</td>
<td>Large size</td>
</tr>
<tr>
<td>Smooth border</td>
<td>Spiculated border</td>
</tr>
<tr>
<td>Diffuse calcification</td>
<td>No or irregular calcification</td>
</tr>
<tr>
<td>Stability over time</td>
<td>Growth over time</td>
</tr>
</tbody>
</table>

Which one is malignant?
So you see a nodule on CXR…

• 1. Is it actually a nodule?
So you see a nodule on CXR…

- 1. Is it actually a nodule?

- 2. Look for prior films?

- 3. Is diffuse calcification present?
Dual energy subtraction x-ray

So you see a nodule on CXR…

- 1. Is it actually a nodule?
- 2. Look for prior films?
- 3. Is diffuse calcification present?
- 4. Get a CT scan or a follow-up CXR

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
<th>CXR features</th>
<th>Common causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar</td>
<td></td>
<td>• Confluent opacities</td>
<td>• Edema</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Air bronchograms</td>
<td>• Acute lung injury</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fluffy edges</td>
<td>• Infection</td>
</tr>
<tr>
<td>Interstitial</td>
<td>Nodules</td>
<td>• Small, well-defined nodules</td>
<td>• Tuberculosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Opacities not confluent</td>
<td>• Fungal infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Normal lung between nodules</td>
<td>• Actinomycetes</td>
</tr>
<tr>
<td></td>
<td>Lines (kerley-b)</td>
<td>• Thin, fine, delicate lines</td>
<td>• Sarcoidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lines at periphery of lung (kerley-b)</td>
<td>• Pulmonary edema</td>
</tr>
<tr>
<td></td>
<td>Lines (reticular)</td>
<td>• Thick, wavy, irregular lines</td>
<td>• Cancer</td>
</tr>
<tr>
<td>Airways</td>
<td></td>
<td>• Circular or tubular</td>
<td>• Fibrotic lung disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thin or thick walled</td>
<td>• Numerous causes</td>
</tr>
<tr>
<td>Not in a single</td>
<td></td>
<td>• One or a few nodules (≤3 cm)</td>
<td>• Lung cancer</td>
</tr>
<tr>
<td>compartment</td>
<td></td>
<td>or masses (&gt;3 cm)</td>
<td>• Metastasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Granuloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Hamartoma</td>
</tr>
</tbody>
</table>
Cardiac & Pulmonary Risk Assessment in the Surgical Patient

Hugo Quinny Cheng, MD
Division of Hospital Medicine
University of California, San Francisco

Preoperative Evaluation Guidelines

Cardiac:

Pulmonary:

Preoperative Cardiac Evaluation

1. Is this patient at increased risk for perioperative cardiac complications?

2. Does the patient need further preoperative medical tests to clarify this risk?

3. What should be done to reduce the risk of cardiac complications?

Clinical Risk Prediction

What increases this patient's risk for perioperative cardiac complications?

70-y.o. man with progressive weakness due to cervical myelopathy need spinal decompression & fusion. He needs help with some ADLs and walks slowly with a cane.

He has stable coronary artery disease & HTN
He is an active smoker.
Question 1: What increases this patient’s risk for perioperative cardiac complications?

1. History of coronary disease
2. History of HTN
3. Current smoker
4. Limited functional status
5. All of the above

Identifying Higher Risk Patients

Heart disease (and equivalents) predicts risk
Heart disease risk factors do not

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td>2.4</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.8</td>
</tr>
<tr>
<td>History of Stroke or TIA</td>
<td>3.2</td>
</tr>
<tr>
<td>Poor functional status</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Surgery Specific Risk

<table>
<thead>
<tr>
<th>Level</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Major aortic or peripheral vascular surgery, Emergent major surgery, Long cases w/ large fluid shifts or blood loss</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Carotid endarterectomy, Head &amp; Neck, Abdominal &amp; Thoracic, Orthopedic</td>
</tr>
<tr>
<td>Low</td>
<td>Endoscopic procedures, Skin &amp; Breast</td>
</tr>
</tbody>
</table>

Revised Cardiac Risk Index

Predictors:
- Ischemic heart disease
- Congestive heart failure
- Diabetes requiring insulin
- Creatinine > 2 mg/dL
- Stroke or TIA
- “High Risk” operation (intraperitoneal, intrathoracic, or suprainguinal vascular)

<table>
<thead>
<tr>
<th># of RCRI</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.4%</td>
</tr>
<tr>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>2</td>
<td>2.4%</td>
</tr>
<tr>
<td>≥ 3</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

RCRI ≥ 2 is “Elevated Risk”
NSQIP Cardiac Risk Prediction Tool

Derived from National Surgical Quality Improvement Program (NSQIP) database:
- > 400,000 patients in derivation & validation cohorts
- Wide range of operations
- "Complication" = 30-day incidence of MI & cardiac arrest

Independent Predictors
1. Type of surgery
2. Age
3. Serum creatinine > 1.5 mg/dL
4. Functional status (dependency for ADLs)
5. American Society of Anesth (ASA) class


What is ASA Classification?

American Society of Anesthesiologists Physical Classification:
1. Healthy, normal
2. Mild systemic disease
3. Severe systemic disease
4. Severe systemic disease that is a constant threat to life
5. Moribund patient not expected to survive without surgery

70-y.o. with h/o CAD, now undergoing cervical spine surgery. Needs help with some ADLs.
- Age 70
- Cr < 1.5
- ASA Class 3
- Partially dependent

Spine surgery

70-y.o. with h/o CAD undergoing cervical spine surgery for progressive weakness.

Estimated risk of perioperative myocardial infarction or cardiac arrest 0.72%

www.qxmd.com/calculate-online/cardiology/gupta-perioperative-cardiac-risk

NSQIP Prediction Tool:
- Excellent performance (AUC = 0.88)
- Doesn’t account for all available information
- ACC/AHA defines risk > 1% as “elevated risk”
Which Prediction Tool is Better?

<table>
<thead>
<tr>
<th></th>
<th>RCRI</th>
<th>NSQIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>~ 4000</td>
<td>~ 400,000</td>
</tr>
<tr>
<td># of hospitals</td>
<td>1</td>
<td>&gt; 200</td>
</tr>
<tr>
<td>Currency of data</td>
<td>1989–94</td>
<td>2007–08</td>
</tr>
<tr>
<td>Screen for MI?</td>
<td>CK-MB, ECG</td>
<td>No</td>
</tr>
</tbody>
</table>

2014 ACC/AHA guideline endorses both tools:
- Elevated risk defined as RCRI > 2 or NSQIP risk > 1%

ACC/AHA: When is Risk Excessive?

- Unstable coronary syndromes
  - Recent MI with post-infarct ischemia
  - Class III or IV angina
- Decompensated CHF
- Significant arrhythmia
  - High grade atrioventricular block
  - Symptomatic ventricular arrhythmia
  - Supraventricular arrhythmia with uncontrolled rate
- Severe valve disease (e.g., critical aortic stenosis)

ACC/AHA: When is Risk Excessive?

Severe or unstable cardiac disease that requires urgent evaluation & treatment, regardless of planned surgery

Utility of Stress Testing

Is further preoperative cardiac testing indicated?

A 63 y.o. man will undergo a Whipple procedure for newly diagnosed pancreatic cancer. He had a remote myocardial infarction, diabetes, and HTN. He has not had chest pain in the past year. Fair functional capacity.

Meds: lovastatin, atenolol, glyburide, benazapril, ASA
PEx: BP=115 / 70; HR=60; normal heart & lung exam
ECG: NSR, LVH, otherwise normal
Question 2:

63 y.o. man s/f Whipple procedure. Remote MI, long-standing diabetes & HTN. No chest pain.

Should this patient receive further preoperative tests?
1. No further testing
2. Yes, perform a stress test

Noninvasive Stress Testing

Predictive value:
- Mainly studied in vascular surgery patients
- Strong negative predictive value ~ 98% (neg LR = 0.1 - 0.2)
- Weak positive predictive value ~10 - 20% (pos LR = 2 - 3)
- Adds little information to lower risk patients
- More useful for cases with increased risk

2014 ACC/AHA Guideline

Revascularization

Should this patient have coronary revascularization?

A 63 y.o. man pancreatic cancer is being considered for a Whipple procedure. History of remote MI, diabetes, HTN. No chest pain in the past year. Fair functional capacity. Persantine-Mibi last year showed mild inferior reversibility. Coronary cath showed a 75% RCA lesion and normal LVEF. He did not receive PCI.
Question 3:

63 y.o. man with CAD undergoing Whipple procedure. His P-Mibi showed mild inferior reversibility. Angiogram showed a 75% RCA lesion and normal LVEF.

Should this patient have coronary revascularization?

1. No, proceed to surgery
2. Consult cardiologist for possible PCI

Carp Trial: Coronary Artery Revascularization Prophylaxis

510 patients undergoing vascular surgery
- At least 1 vessel with 70% occlusion
- Excluded left main dz, AS, or LVEF < 20%

Choice of CABG or PCI plus Medical management
- Medical management alone

1° Endpoint: Long-term mortality
2° Endpoint: MI, Stroke, Limb loss, Dialysis

CARP: Complications After CABG or PCI

<table>
<thead>
<tr>
<th>Complication</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1.7%</td>
</tr>
<tr>
<td>MI</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

CARP: Outcomes After Vascular Surgery

<table>
<thead>
<tr>
<th>Complication</th>
<th>Revascularized (n=225)</th>
<th>Med Mgt Only (n=237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death before surgery</td>
<td>10 (4%)</td>
<td>1</td>
</tr>
<tr>
<td>Death &lt; 30 days post-op</td>
<td>7 (3%)</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Postoperative MI</td>
<td>26 (12%)</td>
<td>34 (14%)</td>
</tr>
<tr>
<td>Long-term mortality (2.7 yrs after randomization)</td>
<td>70 (22%)</td>
<td>67 (23%)</td>
</tr>
</tbody>
</table>

p = NS for all comparisons

ACC/AHA Guidelines for PCI

- Indications for PCI are same as for nonsurgical patients
- Avoid PCI if antiplatelet drugs will need to be held prematurely
- Delay elective surgery after elective PCI:
  - Bare metal stent: 30 days
  - Drug eluting stent: 6 months (optimal)
    - 3 months (if harm in delay)
- Continue or restart antiplatelet agents (especially ASA) as soon as possible, unless bleeding risk precludes

Medical Management

Question 4: Which medication(s) should before surgery?
80-y.o. woman with a remote stroke, diabetes, and HTN will undergo repair of hip fracture. She has been out of care, and she is not taking any medications other than metformin for diabetes.

1. Metoprolol
2. Aspirin
3. Atorvastatin

Rise & Fall of Beta-blockers

- Early trials showed that starting beta-blockers prevented postoperative MI and reduce mortality
- Subsequent studies less impressive, and some positive studies discredited for fraud
- Largest study found small benefit on MI prevention, but increased overall mortality

POISE Trial Results

<table>
<thead>
<tr>
<th>CV Death, Cardiac Arrest, Nonfatal MI</th>
<th>Total Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Metoprolol XL</td>
<td></td>
</tr>
</tbody>
</table>

Metoprolol XL:
Reduced cardiac events (mostly nonfatal MI) but increased risk of stroke & total mortality

Lancet, 2008; DOI: 10.1016/S0140-6736(08)60601-7
2014 ACC / AHA Guideline for β-blockers

Definite indications to continue if... (Helps)
• Already using β-blocker to treat angina, HTN, arrhythmia

Reasonable to consider initiation if... (Maybe)
• High clinical risk (RCRI score > 3)
• Ischemia seen on preoperative stress test
• Compelling indication for long-term beta-blockade

Avoid initiation... (Harms)
• On day of surgery

POISE 2: Aspirin Results

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Placebo</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>7.0%</td>
<td>7.1%</td>
<td>0.99 (NS)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>6.2%</td>
<td>6.3%</td>
<td>0.98 (NS)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>4.6%</td>
<td>3.8%</td>
<td>1.23 (p = 0.04)</td>
</tr>
</tbody>
</table>

Devereaux, PJ et al. NEJM 2014; 370:1484-03

POISE 2 – Patients with PCI

Non-prespecified analysis of subgroup of the 470 patients with history of prior PCI:

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Placebo</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>6.0%</td>
<td>11.5%</td>
<td>0.50 (p = 0.036)</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>5.1%</td>
<td>11.0%</td>
<td>0.44 (p = 0.02)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>5.6%</td>
<td>4.2%</td>
<td>1.26 (p = 0.04)</td>
</tr>
</tbody>
</table>


2014 ACC / AHA Guidelines

Aspirin (for patients without stent)
• Not unreasonable to continue ASA in elective surgery if benefits outweigh risks from bleeding (Class 2b)

• Initiation of ASA does not benefit patients undergoing elective noncardiac surgery (Class 3)

**Trial of Statins in Vascular Surgery**

- Placebo: 10.1%
- Fluvastatin XL: 4.8%

Reduced nonfatal MI
No difference in rates of LFT or CPK elevation


**2014 ACC / AHA Guideline (Statins)**

- **Definitely continue if...** (Class I)
  - Patient is already taking statins chronically

- **Reasonable to initiate if...** (Class 2a)
  - Patient is having vascular surgery

- **Not unreasonable to initiate if...** (Class 2b)
  - Patient has elevated clinical risk and is undergoing a moderate or high risk operation


**Take Home Points**

- **Use a validated clinical prediction tool:**
  - RCRI is easy to use & has become the "new standard"
  - NSQIP tool may be more broadly applicable

- **Reserve stress testing for highest risk patients:**
  - Elevated risk and poor functional status
  - Only do stress test if results will change management (e.g., cancel, delay, or modify surgery)

**Beware perioperative coronary revascularization:**

- Indications are the same as for non-surgical patients
- Don’t perform PCI if patient may have upcoming surgery that requires stopping antiplatelet therapy

**Medical management:**

- Only consider beta-blockers in very high risk patients after considering risks, and not immediately before surgery
- Possible role for initiating statin
Preoperative Pulmonary Evaluation

1. Is this patient at increased risk for perioperative pulmonary complications?
2. Does the patient need further preoperative medical tests to clarify this risk?
3. What should be done to reduce the risk of pulmonary complications?

Pulmonary Risk Prediction

What do you recommend for this patient?

A 65 y.o. man is to undergo repair of an abdominal aortic aneurysm. He has COPD and continues to smoke. He denies change in cough, or worsening of his chronic dyspnea when walking uphill.

Exam: Resp Rate 20 O2 sat 95% RA
Lungs: prolonged expiration, no wheeze

Question 5:

65 y.o. man is s/f repair of an AAA. He has COPD and smokes. No change in cough or usual chronic dyspnea.

Which of the following will be helpful?
1. Obtain PFTs
2. Quit smoking first before surgery
3. Incentive spirometry after surgery
Pathophysiology of Postoperative Pulmonary Complications

- Normal
  - Tidal Breathing
  - Closing Volume

- Decreased FRC
  - Incisional pain
  - Anesthesia
  - Supine position

- Abnormally high Closing Volume
  - Age
  - COPD
  - Smoking

Procedure Related Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurosurgery</td>
<td>2.5</td>
</tr>
<tr>
<td>Head &amp; Neck</td>
<td>2.2</td>
</tr>
<tr>
<td>Aortic</td>
<td>6.9</td>
</tr>
<tr>
<td>Thoracic</td>
<td>4.2</td>
</tr>
<tr>
<td>Abdominal</td>
<td>3.0</td>
</tr>
<tr>
<td>Vascular</td>
<td>2.1</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>2.2</td>
</tr>
<tr>
<td>Prolonged surgery</td>
<td>2.3</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Patient Related Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 60 - 69</td>
<td>2.3</td>
</tr>
<tr>
<td>Age 70 - 79</td>
<td>5.6</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.9</td>
</tr>
<tr>
<td>COPD</td>
<td>2.4</td>
</tr>
<tr>
<td>ASA Class ≥ II vs. Class I</td>
<td>Odds ratio = 4.9</td>
</tr>
<tr>
<td>ASA Class ≥ III vs. Class I or II</td>
<td>Odds ratio = 3.1</td>
</tr>
</tbody>
</table>

ASA Class:
- Class I: no systemic disease
- Class II: mild systemic disease
- Class III: severe systemic disease
- Class IV: systemic disease that is a constant threat to life

Respiratory Failure Prediction Tool

- Derived from National Surgical Quality Improvement Program (NSQIP) database:
  - > 400K patients in derivation & validation cohorts
  - Wide range of operations
  - "Respiratory Failure" = on vent > 48 hrs or reintubation

Independent Predictors:
1. American Society of Anesth (ASA) class
2. Functional status (dependency)
3. Type / location of surgery
4. Emergency surgery
5. Preoperative sepsis or SIRS

Respiratory Failure Prediction Tool

- Emergency surgery? No
- ASA Class 3 (severe systemic)
- Function/dependency: Independent
- Surgery type: Aortic
- Sepsis or SIRS? No

Estimated risk of postoperative respiratory failure: 6.7%

Pulmonary Function Tests & Spirometry

PFT & spirometry add little to risk assessment:
- Usually just tells you what you already know
- Abnormal chest exam findings more predictive of PPC
- Can’t use results to identify patients with prohibitively high risk of PPC or mortality
- Use as diagnostic tool to evaluate unexplained findings

Preoperative Prevention Strategies

Optimize chronic lung disease
- Treat COPD exacerbation (steroids, antibiotics)

Smoking cessation
- Limited evidence for benefit for PPC but other benefits
- May require 8 weeks of cessation for benefit

Respiratory conditioning
- Education on lung expansion & Inspiratory muscle training
- Benefit seen in RCTs in cardiac surgery
Preoperative Smoking Cessation Counseling

RCTs of Preoperative Smoking Cessation Counseling:
1. 120 patients undergoing arthroplasty in 6-8 weeks
2. 60 patients undergoing colorectal resection in 2-3 weeks

Intervention: Smoking cessation counseling & offer free nicotine replacement products

Outcomes: Postop complications, especially wound related (e.g., dehiscence, infection, hematoma)

Smoking Cessation 6-8 Weeks Before TKA or THA

Moller et al. Lancet, 2002

Smoking Cessation 2-3 Weeks Before Colorectal Surgery


Postoperative Prevention Strategies

Lung expansion maneuvers
- Deep breathing or incentive spirometry recommended, though quality of evidence poor
- Consideration of CPAP for very high risk patients

I COUGH – a multi-intervention strategy to prevent PPC
- Incentive spirometry, Coughing & deep breathing, Oral care, Understanding, Get out of bed tid, Head of bed elevated
- Reduced postop pneumonia and unplanned reintubation

Causes of Postoperative Hypoxemia

Upper airway obstruction
- Early onset - often POD 0 or prior to leaving PACU
- Airway edema, vocal cord injury, laryngospasm, OSA

Atelectasis
- Often onset POD 1-2
- Secretion management: chest therapy, pulmonary toilet
- Positive airway pressure: CPAP, BiPAP, EzPAP

Pulmonary edema
- Often onset by POD 2
- Cardiogenic vs. non-cardiogenic

Pneumonia
- Most common in first 5 days postop (unless on ventilator)
- Think Staph aureus & gram negative rods
- Pseudomonas? Risk with ≥ 5 days hospitalization or prior antibiotic exposure, dialysis, nursing home

Other etiologies:
- Pulmonary embolism
- Bronchospasm
- Effusions – common after abdominal surgery, usually small, exudative and usually don’t require treatment

Take Home Points

Patient related risks:
- Elderly
- COPD
- Severe medical comorbidity
- Functionally dependent or generally debilitated

Procedure related risks:
- Thoracic surgery
- Abdominal surgery
- Emergency surgery
- Prolonged surgery > 3 hrs
- General anesthesia

Pulmonary function tests:
- Should not be done routinely
- Consider to help evaluate unexplained symptoms

Risk reduction:
- Patients at increased risk for pulmonary complications should receive lung expansion maneuvers
- Smoking cessation likely beneficial but may require two months lead time to be effective
Thank You

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NOTES
Session Outline

*Point-of-Care Ultrasound (POCUS) is the future of the physical exam*

- Questions we’ll address around this topic:
  - What is POCUS for hospitalized patients?
  - Why learn POCUS?
  - How POCUS is used (cases + demo)?
  - How to get started with POCUS (for you & your institution)?

What is POCUS?

- Performed and interpreted by primary provider…
- …at the bedside…
- …to help answer a specific clinical question…
- …quickly

Disclosures

- Consultant for Caption Health
How we use POCUS in Hospital Medicine?

- Diagnostic
- Therapeutic (procedural guidance)
- Treatment monitoring
- Disease screening

Why learn POCUS?

**Reason 1: It makes you a better doctor**

- Procedural complications
- Efficiency and accuracy of diagnosis
- Patient satisfaction

**Reason 2: Most IM/HM doctors don’t know much….**

(Especially if you trained awhile ago)

**Reason 3: Despite lack of knowledge, people think its important….**

2017 Needs Assessment of UCSF Hospitalists

- 93% I believe POCUS is important for diagnostic purposes in internal medicine.
- 88% I believe POCUS should be a formal part of residency training.
- 93% I believe faculty would benefit from faculty development in POCUS.
Why learn POCUS?

Its coming whether you like it or not...

Cases: Inpatient Care as a POCUS Hospitalist

- Four common inpatient scenarios
  - Brief HPI and exam
  - Demo image acquisition and review normal anatomy/findings
  - Review abnormal images from the case
  - Discuss how POCUS impacted care delivery

---

Case 1: Mr. Seth is short of breath

- HPI: 61 M w/ HFrEF, COPD admitted for COPD exacerbation & CAP.
  - → nebulizers, prednisone, and antibiotics
  - HD #3: increasing respiratory distress and anxiety
- Vitals: AF, HR 102, BP 192/97, RR 26, O2 sat 82% on RA → 93% on 6L NC
- Exam:
  - General: moderate distress.
  - CV: Tachycardic, no MRG. Unable to assess JVP. 1+ pitting edema of b/l LEs.
  - Lung: tachypneic, increased WOB, scattered wheeze with bilateral lower lobe rales.
- Labs: normal CBC and BMP; BNP 421, Tnl pending, EKG non-ischemic. CXR ordered.

+ POCUS!

On admission, →3 b-lines in R anterior lung, otherwise normal.

Now, diffuse b-lines in bilateral lung fields, bilateral pleural effusions. IVC 2.4cm and minimally collapsible.
Demo: Lung Ultrasound (LZ 1-3)

 Demo: Lung Ultrasound (LZ 4)

Demo: IVC Ultrasound

- **B-lines**
  - Pattern helps you with ddx:
  - Bilateral (interstitial syndrome) vs Focal
  - Higher sensitivity than CXR
  - Useful for dynamic monitoring
- Pleural effusion
  - Anechoic space (black) surrounded by anatomic borders
  - Spine sign
  - Simple vs. complex
  - Sensitivity > CXR

- IVC
  - Dilated >2cm
  - Non-collapsible <50%
  - In a dyspneic patient:
    - >80% sensitivity & specificity for HF/volume overload
    - Most confusing/controversial POCUS exam

Case 1 Resolution
- POCUS diagnosis: interstitial syndrome, pleural effusions, volume overload
- You give him IV Lasix and treat his blood pressure → BP normalized and hypoxia improving
- You make a mental note to check his lung and IVC US again tomorrow to decide about thoracentesis and further need for diuretics

Case 1 Take Home Points
- POCUS
  - improved the quality of your index exam
  - helped you quickly identify why his condition acutely changed
- When possible:
  - Have an algorithmic approach
  - Combine multiple pcus exams and integrate with other data

Kajimoto et al, Cardiovascular Ultrasound, 2012.
Case 2: Mrs. Essig is hypotensive

- **HPI:** 52W with metastatic breast cancer c/o L malignant pleural effusion on chemotherapy p/w generalized weakness, dyspnea, lethargy, HR 123 BP 82/40
  - 2L given 2L BVF with improvement.
- **Vitals:** AF, HR 112, BP 90/47, RR 16, O2 sat 96% on RA
- **Exam:**
  - General: arousable but somnolent, comfortable
  - CV: Tachycardic, regular, no MRG. JVP 6cm. Chronic lymphedema of the b/l LEs
  - Lung: breathing comfortably on RA, diminished breath sounds LLB but otherwise CTA bilaterally
- **Labs:** CBC and BMP normal. Tbi 1.6, normal AST/ALT. BNP 235 (unknown baseline). TnI negative.

**POCUS!**

- Cardiac US with mildly reduced LVEF, pericardial effusion, Lungs with a-lines throughout, moderate bilateral L pleural effusion, IVC 1.8cm with ~50% collapse with inspiration.
**LV Ejection Fraction**
- Evaluation:
  - End-point Septal Separation (EPSS)
  - Fractional Shortening
  - Myocardial Thickening
- Qualitative assessment:
  - Hypodynamic
  - Normal
  - Mild-moderately reduced
  - Severely reduced
- LV dysfunction by hospitalists: 91% sensitivity, 88% specificity

**Pericardial Effusion**
- Qualitative assessment:
  - Small
  - Moderate
  - Large
- Pericardial effusion by hospitalists: 100% sensitivity, 87% specificity

**Case 2 Resolution**
- POCUS diagnosis: new mild-moderate LVEF reduction, new small pericardial effusion
- Repeat TTE on HD#1 confirms new EF 40%, pericardial effusion enlarging
- HD#3 she develops tamponade, undergoes pericardial drain placement. Patient and family opt for hospice referral.

**Case 2 Take Home Points**
- POCUS led you to a faster, new diagnosis of HFrEF.
  - Clinical management: more cautious with IVF
  - Further diagnostic testing: ordered TTE from admission
  - Monitoring evolution of pericardial effusion
  - Assist with prognostication & GOC

*Table 4: Diagnostic capabilities of real-time ultrasound POCUS compared to standard echocardiography in the evaluation of cardiac tamponade.*

<table>
<thead>
<tr>
<th>Condition</th>
<th>POCUS [n=121]</th>
<th>Echocardiography [n=121]</th>
<th>p-value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Tamponade</td>
<td>83 (69.1%)</td>
<td>100 (82.9%)</td>
<td>0.15</td>
<td>0.95</td>
<td>0.85</td>
<td>2.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Pericardial effusion, moderate to large</td>
<td>33 (27.2%)</td>
<td>50 (41.2%)</td>
<td>0.03</td>
<td>0.87</td>
<td>0.77</td>
<td>4.0</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Case 3: Dr. Nye has an AKI

- **HPI**: 84M with BPH, HTN, DM2 presents with AMS, lower abdominal pain, decreased urination, K 6.4. ED POCUS shows hydronephrosis and a distended bladder
  - Foley with 400cc urine output. HyperK treatment.

- **Vitals**: within normal limits

- **Exam**:
  - General: mildly agitated but redirectable, no distress
  - Abdominal: suprapubic tenderness, no CVA tenderness, no distension, NABS
  - GU: Foley in place draining cloudy yellow urine

- **Labs**: WBC 11.7, BUN 48, Cr 2.6, K 6.1, otherwise normal. UA +WBC, +nitrite, +LE, +blood. Urine culture pending, CTAP pending.

**POCUS**

- **Renal US**: Bilateral hydronephrosis
- **Bladder**: still distended with Foley balloon visible
- **IVC**: 1.4 cm, collapsible with inspiration
- **FAST**: negative for free fluid
- **WBC**: 14K, slightly left shifted
Demo: Bladder Ultrasound

- **Hydronephrosis**
  - Arises from renal pelvis and extends through kidney
  - Grading:
    - Mild-moderate
    - Severe

- **Bladder Volume**
  - Measure in transverse and longitudinal planes
  - \( L \times W \times H \times 0.5 \)

---

**Case 3 Resolution**

- POCUS diagnosis: severe hydronephrosis, foley dysfunction with urinary retention
- Foley is flushed and repositioned \(\rightarrow\) additional 800cc urine output. He is started on ceftriaxone for UTI and Tamsulosin for BPH. His abdominal pain resolves; you cancel the CT scan.
- HD #2: urine culture + for pan-sensitive E Coli \(\rightarrow\) abx narrowed to cephalaxin K, Cr improved. Foley is removed and he passes a trial of void prior to discharge.
Case 3 Take Home Points

- POCUS helped you quickly identify a complication in your treatment plan
  - Avoided a potential bad outcome & unnecessary CT scan.
- Accuracy of bladder volume by POCUS > bladder scan
- Detecting hydronephrosis is a readily attainable skill
  - IM residents x5 hrs of renal US practice = 94% sensitivity; 93% specificity for moderate-severe hydronephrosis

Case 4: Ms. Nidus has cellulitis

- HPI: 36Y with IVDU, DVT not on anticoagulation presents Saturday night with a red, swollen, and painful RLE. No fevers or chills.
  - IV, empiric antibiotics for cellulitis and orders a RLE Doppler
- Vitals: Afebrile, HR 98, BP 108/55, RR 16, O2 sat 98% RA
- Exam:
  - General: awake, alert, cooperative. In mild distress 2/2 pain.
  - CV: RRR, no MRG.
  - MSK: RLE tender, erythematous, warm to touch distally. No fluctuance or purulence. She is diffusely TTP overlying the area. Mild pitting edema of R>LLE. intact pulses.
- Labs: WBC 12.3, CBC otherwise normal. Lactate 2.1, D-dimer 785. Doppler RLE is ordered, but won’t be performed until the techs arrive on Monday morning.

How many people would anticoagulate her?

Demo: Soft Tissue Ultrasound
Demo: DVT US

SSTI
- Cobblestoning (cellulitis)
- Deep fluid pocket (abscess)
- Hospitalists ID’ing abscess: 97% sensitivity, 84% specificity

DVT US
- Compression-only
- 5 branch points (including popliteal)
- Sensitivity 100%, specificity 95%
  compared to radiology

Case 4 Resolution
- POCUS diagnosis: cellulitis, no abscess, +DVT. Safe for further fluid resuscitation.
- You give an additional 1L IVF → lactate, BP normalizes
- You start her on therapeutic lovenox for DVT seen on POCUS, confirmed by radiology DVT study 36 hours later.
- She tolerates oral antibiotics well, cellulitis improves. Prior to discharge, switch to oral DOAC with plans to follow up with a community PCP.
Case 4 Take Home Points

- In a resource-limited environment (overnights, weekends) POCUS can lead to faster initiation of appropriate therapy
- POCUS can help guide fluid resuscitation in the setting of hypotension or tachycardia.
- Just because you POCUS, doesn’t mean you can’t order the formal study!

So why do we POCUS?

- Earlier diagnosis and treatment
- Avoids additional tests and reduces radiation exposure
- Safe treatment monitoring, prognostication
- Skills are attainable and lead to better quality care delivery than exam alone

POCUS doesn’t replace the physical exam; it enhances the physical exam.

It IS the physical exam

Data for the POCUS we covered

<table>
<thead>
<tr>
<th>Exam</th>
<th>Statistical Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC</td>
<td>Correlation coefficient 0.7-0.9</td>
</tr>
<tr>
<td>LVEF</td>
<td>LR +5.4; LR -0.2</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>LR +7.7; LR -0.0</td>
</tr>
<tr>
<td>Pulmonary Edema</td>
<td>Sensitivity 94%; Specificity 92%</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>Sensitivity 93%; Specificity 96%</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>Sensitivity 94%; Specificity 93%</td>
</tr>
<tr>
<td>DVT</td>
<td>Sensitivity 100%; Specificity 96%</td>
</tr>
<tr>
<td>Abscess</td>
<td>Sensitivity 97%; Specificity 84%</td>
</tr>
</tbody>
</table>

Data for POCUS Algorithms

- **Rapid Ultrasound in Shock and Hypotension (RUSH)**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Diagnosis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A lines (normal)</td>
<td>Asthma/COPD</td>
<td>89</td>
<td>97</td>
</tr>
<tr>
<td>Diffuse B lines (&gt;2 lung zones)</td>
<td>Pulmonary edema</td>
<td>97</td>
<td>96</td>
</tr>
<tr>
<td>Loss of pleural line, consolidation, patchy B lines</td>
<td>Pneumonia</td>
<td>95</td>
<td>94</td>
</tr>
<tr>
<td>Abscess without pleural sliding, lung point</td>
<td>Pneumothorax</td>
<td>81</td>
<td>75</td>
</tr>
</tbody>
</table>

- **BLUE protocol for dyspnea/hypoxia**
What is the scope of POCUS in HM?

Soni et al, “Point-of-Care Ultrasound for Hospitalists: A Position Statement of the Society of Hospital Medicine.” JHM 2019

How should you integrate POCUS into your practice?

- Many factors to think through:
  - Context
  - Frequency
  - Difficulty
  - Data

Addressing Barriers

- Hardware
- Training
- Time and money constraints
- Credentialing and privileging
POCUS Learning Pathways

- Pursue a certificate program (SHM, CHEST)
- Attend workshops (SHM, ACP, AIUM, UCSF)
- Learn from local experts (EM, critical care colleagues)
- Self-learning, ad hoc (FOAMed)

Soni et al. Cert of POCUS. JHM 2017

Our institution’s experience

Getting started…

- Champion(s)
- Leadership buy-in
  - Education
  - Research
  - Cost savings
  - Clinical outcomes

Our institution’s experience

Building momentum…

- Training program development
- Equipment investment

Level 1: Basic Knowledge
  - Portfolio building & Credentialing

Level 2: Early User
  - Scanning Sessions, Workshops

Level 3: Independent Use
  - Modules, Didactics

Conner et al, POCUS Journal, in press.

Making it official

1. Privileging and Credentialing
2. Quality assurance
3. Integration into EMR and billing

IMAGE HERE: Notary stamp?
"The larger issue now is to decide whether we believe that – in this case hospitalists – building competency in ultrasound among generalist physicians will enhance patient safety, quality, and value. **Personally, I do.**"

- Bob Wachter, 2012

---

**Review of Session Goals**

- What is POCUS for hospitalized patients?
- Why learn POCUS?
- How POCUS is used (cases + demo)?
- How to get started with POCUS (for you & your institution)?

**POCUS is the future of the physical exam.**

---

**Questions?**

- Trevor.Jensen@ucsf.edu
High Yield Neurological Examination

Vanja Douglas, MD
Sara & Evan Williams Foundation Endowed Neurohospitalist Chair
Director, Neurohospitalist Division
Associate Professor of Clinical Neurology
UCSF Department of Neurology

Purpose of Neuro Exam

• Screen asymptomatic patients
• Screen patients with symptoms that could indicate a focal neurologic lesion (e.g. back pain, headache, seizure)
• Localize the lesion in patients with neurologic deficits
  • Generate a differential diagnosis
  • Decide what test to get next (e.g. brain MRI, spine MRI, EMG/NCS, CK)

Typical “Screening” Neuro Exam

• Mental Status: Level of alertness, orientation, attention, language, memory
• Cranial Nerves: II through XII
• Motor: Bulk, tone, power in all muscles in both arms and legs
• Sensory: Light touch, vibration/joint position sense, pain/temperature, Romberg
• Reflexes: Biceps, triceps, brachioradialis, knees, ankles, plantar response
• Coordination: Finger-nose-finger, heel-knee-shin
• Gait: Observe gait, include tandem, heel, and toe walking

Disclosures

None
High Yield Screening Neuro Exam

- Mental Status
- Cranial Nerves
- Motor
- Sensory
- Coordination
- Reflexes
- Gait

Language

<table>
<thead>
<tr>
<th>Aphasia Type</th>
<th>Fluency</th>
<th>Comprehension</th>
<th>Repetition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expressive</td>
<td>Impaired</td>
<td>Intact</td>
<td>Impaired</td>
</tr>
<tr>
<td>Conduction</td>
<td>Intact</td>
<td>Intact</td>
<td>Impaired</td>
</tr>
</tbody>
</table>

Receptive Aphasia

<table>
<thead>
<tr>
<th>Aphasia Type</th>
<th>Fluency</th>
<th>Comprehension</th>
<th>Repetition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>Impaired</td>
<td>Impaired</td>
<td>Impaired</td>
</tr>
</tbody>
</table>

Extraocular Movements

- SR
- IO
- MR
- LR
- IR
- SO
Facial Symmetry

Visual Fields

High Yield Screening Neuro Exam

- Mental Status: language, orientation, and attention
- Cranial Nerves: visual fields, eye movements, and facial symmetry
- Motor
- Sensory
- Coordination
- Reflexes
- Gait

Motor System

2 minute screen for upper motor neuron weakness:

- Pronator Drift
- Finger taps & Foot taps
- Distal extensor power:
  - Finger extensors
  - Tibialis anterior
High Yield Screening Neuro Exam

• Mental Status: language, orientation, and attention
• Cranial Nerves: visual fields, eye movements, and facial symmetry
• Motor: Pronator drift, finger and foot taps, finger extensor and extensor hallucis longus power
• Sensory
• Coordination
• Reflexes: Biceps, knees, and ankles
• Gait

Why Do A Sensory Exam?

• If there are sensory complaints
• If there are balance complaints or a gait disorder
• If there is weakness

Coordination & Gait

• Hemispheres:
  • Finger-nose-finger
  • Heel-knee-shin
• Vermis:
  • Gait
High Yield Screening Neuro Exam

- Mental Status: language, orientation, and attention
- Cranial Nerves: visual fields, eye movements, and facial symmetry
- Motor: Pronator drift, finger and foot taps, finger extensor and extensor hallucis longus power
- Sensory: (If done, do pain OR temp + vibration OR JPS)
- Coordination: Finger-nose-finger and heel-knee-shin (can replace HKS with gait)
- Reflexes: Biceps, knees, and ankles
- Gait: Observe gait (base, stride, posture, arm swing, turn), tandem

Think Like A Neurologist

- Chief Complaint: suspected localization
- History: refine the localization
- Exam: pick maneuvers that rule in or rule out your suspicions

Let’s practice!

Case Scenarios
Patient #1

• A 23 y/o woman with a history of migraine headaches is admitted to the hospital with left leg cellulitis. On hospital day 2, she complains of a new headache. She says it’s different from her previous migraines because it is “much worse” and is wondering if she needs an MRI.

Headache

Suspected localization
• Focal brain lesion

Patient #2

• 57 y/o man hospitalized with MI is altered after his cardiac cath. He is somnolent but arousable, mumbling incoherently. His family is very concerned that he has had a stroke.
Altered Mental Status

Suspected localization
• Bilateral hemispheres
• Brainstem

Patient #2 Exam

• Arouses to touch
• Names simple objects, repeats short phrases, follows simple commands
• Disoriented and unable to test attention
• EOMI; face symmetric; blinks to threat bilaterally
• Left arm drifts and hand is clumsy
• Withdraws less briskly to pain in the left leg
• Head CT is normal

Multifocal Strokes

Patient #3

• A 65 y/o man with prostate cancer presents with bilateral leg weakness and urinary urgency.
Bilateral Leg Weakness

**Suspected localization**
- Spinal cord
- Cauda equina
- Neuropathy
- Neuromuscular junction
- Muscle

<table>
<thead>
<tr>
<th></th>
<th>UMN</th>
<th>LMN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pattern of Weakness</strong></td>
<td>Paresis</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Function/Recumbency</strong></td>
<td>More alternate motion rate</td>
<td>Impairment of function is mostly due to weakness</td>
</tr>
<tr>
<td><strong>Tone</strong></td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Tendon Reflex</strong></td>
<td>Increased</td>
<td>Decreased, absent or normal</td>
</tr>
<tr>
<td><strong>Other signs</strong></td>
<td>Babinski sign, other CNS signs (e.g., ataxia, visual field cut)</td>
<td>Atrophy (except with problem of neuromuscular junction)</td>
</tr>
</tbody>
</table>

---

**Spinal Cord Cross-Section**

**Patient #3: Exam**
- Decreased EHL power bilaterally
- Slow foot taps
- Brisk knee jerk and ankle jerk reflexes
- Reduced joint position sense in toes
- Sensory level to pinprick at T5
Metastatic Spinal Cord Compression

Patient #4

- A 30 y/o woman with lupus, APLAS, and history of endocarditis on gentamycin presents with acute vertigo.

Vertigo

**Suspected localization**
- Brainstem (central)
- Cerebellum (central)
- Inner ear (peripheral)

Hypothesis-Driven Neuro Exam
**HINTS**

- Head Impulse Test
  - Abnormal = peripheral
- Nystagmus
  - Unidirectional = peripheral
  - Direction-changing = central
- Test of Skew
  - Skew deviation = central
- [https://youtu.be/1q-VTKPweuk](https://youtu.be/1q-VTKPweuk)

**Patient #4: Exam**

- Left beating nystagmus in left-gaze only
- Positive head thrust test to the right

**Gentamycin Toxicity**

**Summary**

- High yield screening exam
- Hypothesis driven approach to:
  - Suspected focal brain lesion
  - Altered mental status
  - Suspected spinal cord lesion
  - Vertigo
**Bonus Case**

- A 32 y/o woman presents with tingling in the hands and feet that progressed to diffuse weakness in the arms and legs over four days. She is now so weak she can no longer sit up.

**Diffuse Weakness**

**Suspected localization**
- High spinal cord
- Neuropathy
- Neuromuscular junction
- Myopathy

**Localization of Weakness**

<table>
<thead>
<tr>
<th>Pattern of weakness</th>
<th>Tone</th>
<th>Bulk</th>
<th>Reflexes</th>
<th>Sensory Loss</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Motor Neuron</td>
<td>Pyramidal</td>
<td>Spastic</td>
<td>Normal</td>
<td>Increased</td>
<td>Varies</td>
</tr>
<tr>
<td>Anterior Horn Cell</td>
<td>Pyramidal or myotomal</td>
<td>Spastic or normal</td>
<td>Atrophy</td>
<td>Increased or decreased</td>
<td>None</td>
</tr>
<tr>
<td>Peripheral Nerve</td>
<td>In distribution of root or nerve</td>
<td>Normal or reduced</td>
<td>Atrophy</td>
<td>Decreased</td>
<td>Prominent</td>
</tr>
<tr>
<td>Neuromuscular Junction</td>
<td>Diffuse</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal (myasthenia) or Absent (botulism)</td>
<td>None</td>
</tr>
<tr>
<td>Muscle</td>
<td>Proximal &gt; Distal</td>
<td>Normal</td>
<td>Normal or pattern atrophy</td>
<td>Normal</td>
<td>None</td>
</tr>
</tbody>
</table>
Next Step?

• Lumbar puncture:
  • Protein 143
  • WBC 2
• Guillain-Barre Syndrome

Acknowledgements

• Hooman Kamel
• Andy Josephson
• Dan Lowenstein
• Ann Poncelet
Algorithmic Approach to Lung Opacities

Approach to lung opacities

• This is hard!
• You will not be an expert today
• Approach
• Practice
• Think like a pathologist

Categories of lung opacities

• 1. Consolidation
• 2. Interstitial (diffuse lines or nodules)
• 3. Airways
• 4. One or a few nodules
Alveolar

Interstitial

Airways

Not applicable
• Consolidation
• Confluent opacity
• Fluffy around periphery
• Air bronchograms
• Lack of volume loss
Consolidation

- Acute vs. chronic symptoms
- Distribution
- Acuity of changes
- Differential diagnosis in acute setting
  - Focal: pneumonia/aspiration, hemorrhage
  - Diffuse: edema, acute lung injury, pneumonia, hemorrhage

Invasive mucinous adenocarcinoma
Chronic alveolar disease

- Tumor
  - Invasive mucinous adenocarcinoma (aka multifocal bronchoalveolar CA)
  - Lymphoma (recurrent or 1° pulmonary)
- Inflammatory
  - Organizing pneumonia
  - Chronic eosinophilic pneumonia
  - Sarcoidosis
- Other
  - Lipoid pneumonia
  - Alveolar proteinosis

Comparison

Signs of atelectasis: volume loss

- Fissure displacement
- Deviation of mediastinal structures
- Elevated diaphragm
Rapid change

Atelectasis (types)

- Obstructive/resorptive (obstruction of bronchus)
- Passive (compression of lungs)
- Cicatricial (related to scarring)
- Adhesive (surfactant deficiency)
Lung cancer (Golden S sign)

Lower lobe atelectasis

Combined RML/RLL atelectasis
Left upper lobe collapse

1. Veil-like density
2. Volume loss
   – Elevated diaphragm
   – Elevated left PA
• Luftsichel sign

Interstitial opacities

Nodules: diff dx

• Hematogenous spread
  – Miliary tuberculosis
  – Miliary fungal infection (e.g. coccidioidomycosis)
  – Metastases
• Lymphatic spread
  – Sarcoidosis
  – Lymphangitic spread of tumor
  – Pneumoconioses (e.g. silica)
Histoplasmosis

Miliary tuberculosis

Interstitial: lines

Causes of interstitial lines

- Edema
- Malignancy
- Fibrotic lung diseases (this is a long list)

Kerley-b lines may be present

These lines are typically thick, wavy and irregular
Reticular opacities (distribution)

- Lower lobe predominant
  - Idiopathic pulmonary fibrosis
  - Connective tissue disease
  - Drugs
  - Asbestosis
  - Hypersensitivity pneumonitis
- Upper lobe predominant
  - Sarcoidosis
  - Prior TB/fungus
  - Pneumoconioses
Airways disease

• Circular

• Tubular
Differential diagnosis of airways disease

- Mild:
  - Asthma
  - Viral infection
  - Chronic bronchitis
  - Etc.

- Severe:
  - Bronchiolitis obliterans
  - Immunodeficiency
  - Ciliary dyskinesia
  - Cystic fibrosis
  - ABPA
  - Tuberculosis
  - Cartilage diseases

Cystic fibrosis

Which compartment of lung is affected?

Solitary pulmonary nodule: differential diagnosis

- Granuloma
- Hamartoma
- Primary bronchogenic carcinoma
- Metastasis
- Lots of others
Which one is malignant?

Nodules: benign vs. malignant

<table>
<thead>
<tr>
<th></th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Small size</td>
<td>Large size</td>
</tr>
<tr>
<td><strong>Border</strong></td>
<td>Smooth border</td>
<td>Spiculated border</td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td>Diffuse calcification</td>
<td>No or irregular calcification</td>
</tr>
<tr>
<td><strong>Stability over time</strong></td>
<td>Stability over time</td>
<td>Growth over time</td>
</tr>
</tbody>
</table>
So you see a nodule on CXR…

- 1. Is it actually a nodule?
So you see a nodule on CXR…

1. Is it actually a nodule?
2. Look for prior films?
3. Is diffuse calcification present?
So you see a nodule on CXR…

1. Is it actually a nodule?

2. Look for prior films?

3. Is diffuse calcification present?

4. Get a CT scan or a follow-up CXR

### Algorithmic Approach to Lung Opacities

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
<th>CXR features</th>
<th>Common causes</th>
</tr>
</thead>
</table>
| Alveolar          |             | • Confluent opacities  
|                   |             | • Air bronchograms  
|                   |             | • Fluffy edges                                                             | • Edema  
|                   |             |                                                                              | • Acute lung injury  
| Interstitial      | Nodules     | • Small, well-defined nodules  
|                   |             | • Opacities not confluent  
|                   |             | • Normal lung between nodules                                               | • Tuberculosis  
|                   | Lines (kerley-b) | • Thin, fine, delicate lines  
|                   |             | • Lines at periphery of lung (kerley-b)                                      | • Fungal infection  
|                   | Lines (reticular) | • Thick, wavy, irregular lines                                               | • Metastases  
| Airways           |             | • Circular or tubular  
|                   |             | • Thin or thick walled                                                      | • Sarcoidosis  
| Not in a single compartment | | • One or a few nodules (<3 cm) or masses (>3 cm)                             | • Pulmonary edema  
|                   |             |                                                                              | • Cancer  
|                   |             |                                                                              | • Fibrotic lung disease  
|                   |             |                                                                              | • Numerous causes  
|                   |             |                                                                              | • Lung cancer  
|                   |             |                                                                              | • Metastasis  
|                   |             |                                                                              | • Granuloma  
|                   |             |                                                                              | • Hamartoma  

On to the cases…

### Dual energy subtraction x-ray

So you see a nodule on CXR…

1. Is it actually a nodule?

2. Look for prior films?

3. Is diffuse calcification present?

4. Get a CT scan or a follow-up CXR
Objectives

- Lingering questions from this mornings presentations
- Duration of anticoagulation for VTE
- Approach to subsegmental PE, calf vein DVT and superficial vein thrombosis
- Role of thrombophilia work up
- Resuming anticoagulation after a bleed

Case

51 year old man with no PMHX presents with acute CP and SOB, BP stable, HR 120s O2 sat 92%, d-dimer 1500, CT PE with bilateral PE in all lobes with RV/LV ratio > 1.0. BNP 370, trop 1.5. He is started on rivaroxaban. He has no identifiable provoking factors. How long should he remain on anticoagulation?
1) At least 3 months
2) One year
3) Forever

Resources

- University of Washington Anticoagulation http://depts.washington.edu/anticoag/home
**ESC PE Guidelines—Duration of Therapy**

### DURATION OF AC

<table>
<thead>
<tr>
<th>Indication</th>
<th>CHEST 2019</th>
<th>AC Forum 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st provoked VTE</td>
<td>≥ 3 months</td>
<td>≥ 3 months (staged)</td>
</tr>
<tr>
<td>1st unprovoked VTE</td>
<td>Extended^a</td>
<td>Extended</td>
</tr>
<tr>
<td>2nd unprovoked VTE</td>
<td>Extended^a</td>
<td>Extended</td>
</tr>
<tr>
<td>VTE + cancer</td>
<td>Extended^a</td>
<td>Extended</td>
</tr>
</tbody>
</table>

^aUnless risk factors for recurrence persist

**Recommendations**

- ESC: Suggest indefinite
- CHEST 2019: Recommend AGAINST indefinite
- Weak rec/mod evidence

**VTE and Bleeding Risk: 2016 CHEST Guideline**

<table>
<thead>
<tr>
<th>Risk Factors for Bleeding with Anticoagulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70y</td>
</tr>
<tr>
<td>Previous bleeding</td>
</tr>
<tr>
<td>Cancer</td>
</tr>
<tr>
<td>Renal or hepatic failure</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Previous stroke</td>
</tr>
</tbody>
</table>

**Duration of Anticoagulation for VTE:**

2016 CHEST and AC Forum Guidelines/Guidance

- Indication CHEST 2019 AC Forum 2016
- 1st provoked VTE ≥ 3 months ≥ 3 months (surgical)^b ≥ 3 months (medical)
- 1st unprovoked VTE Extended^a Extended
- 2nd unprovoked VTE Extended^a Extended
- VTE + cancer Extended^a Extended

^aUnless risk factors for recurrence persist
^bNo scheduled stop date, unless high bleeding risk.


---

**Table 1: Estimated risk of venous thromboembolism disease recurrence after anticoagulant discontinuation in patients being monitored using IVC filters**

<table>
<thead>
<tr>
<th>Estimated risk of recurrence</th>
<th>Risk factor</th>
<th>Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Minor bleed</td>
<td>surgery</td>
</tr>
<tr>
<td>Moderate</td>
<td>Major bleed</td>
<td>hormonal, heparinisation</td>
</tr>
<tr>
<td>High</td>
<td>≥ 2 risk factors</td>
<td>Thrombus with embolus</td>
</tr>
</tbody>
</table>

**Risk of Major Bleeding After 3 Mos of Anticoagulation: %/y**

- Baseline risk: 0.3%
- Moderate (1 risk factor): 1.6%
- High (≥ 2 risk factors): 3.6%
- Total risk: 0.8%
CHEST 2021—suggest reduced dose DOAC over full dose for extended phase anticoagulation

UNPROVOKED VTE

- All - 3-6 months of FULL intensity anticoagulation
  - At 3-6 months determine candidacy for secondary prevention
  - ~50% will develop recurrent VTE in 10 years off anticoagulation; Case fatality rate of VTE is ~4% in all comers but closer to 9% in PE
  - Case fatality rate of bleeding is ~10%
  - Case by case decision...consider continuation if not high bleeding risk. Most compelling in low bleed risk patients and those with PE

Secondary Prevention Options
- Low dose DOAC
- Full dose anticoagulation
- ASA

Do not use dose reduced DOAC:
- Cancer
- Recurrent VTE on AC
- Obesity

Case

51 year old man with no PMHX presents with acute CP and SOB, BP stable, HR 120s O2 sat 92%, d-dimer 1500, CT PE with bilateral PE in all lobes with RV/LV ratio > 1.0. BNP 370, trop 1.5. He is started on rivaroxaban. He has no identifiable provoking factors. How long should he remain on anticoagulation?
1) At least 3 months
2) One year
3) Forever
A 77 yo man had undergone colectomy for recurrent bleeding from diverticulosis. On POD #3 he becomes tachycardic to the 110s. WBC is elevated. The surgical team orders an abdominal CT which shows a fluid collection concerning for early abscess. It also shows an isolated RLL subsegmental PE. A dedicated CTa shows a single isolated RLL subsegmental PE. Do you anticoagulate this patient?

a) Sure, it is a PE.

b) No this is incidental. Let’s pretend we don’t know it is there.

Isolated Subsegmental PE

Definition: PE shown on CT angiography that occurred in a subsegmental branch but no larger order of vessels. The subsegmental PE may involve one or more than one subsegmental branch.

Identification of ISSPE has tripled over past decade.

Summary of main results:

There is currently no evidence from randomised controlled trials to assess the effectiveness and safety of anticoagulation therapy versus no intervention in patients with isolated subsegmental pulmonary embolism (ISSPE) or incidental ISSPE.

A 77 yo man had undergone colectomy for recurrent bleeding from diverticulosis. On POD #3 he becomes tachycardic to the 110s. WBC is elevated. The surgical team orders an abdominal CT which shows a fluid collection concerning for early abscess. It also shows an isolated RLL subsegmental PE. Do you anticoagulate this patient?

a) Sure, it is a PE.
b) No this is incidental. Let's pretend we don’t know it is there

A 67 year old man with cirrhosis, new diagnosis of HCC is admitted with diarrhea, lowish BP and AKI. On exam he has bilateral lower extremity swelling, R> L. In the ED he has an ultrasound which shows thrombosis of the greater saphenous vein extending from the calf proximally and terminating 6 cm from the deep femoral vein. What do you recommend?

a. Prophylactic fondaparinux
b. Prophylactic rivaroxaban
c. Full dose DOAC or warfarin
d. Full dose LMWH
e. Warm compresses, no anticoagulation

Factors that favor the use of AC:
- extensive SVT; above the knee, close to saphenofemoral junction; severe symptoms; involvement of the greater saphenous vein; history of VTE or SVT; active cancer; recent surgery
- In patients with superficial vein thrombosis of the lower limb of at least 5 cm in length, we suggest the use of a prophylactic dose of fondaparinux or LMWH for 45 days over no anticoagulation (Grade 2B).
Superficial Vein Thrombosis

Prevention of thromboembolic complications in patients with superficial vein thrombosis given rivaroxaban or fondaparinux: the open-label, randomised, non-inferiority SURPRISE study trial.

- >400 pts symptomatic SVT riva 10 mg v fonda 2.5mg
- Symptomatic above the knee SVT of at least ≥ 5 cm length + other risk factor (>65, male, hx VTE, cancer, autoimmune disease, non-varicose veins)
- No difference in primary efficacy outcome
- After 6 weeks 7% recurrence risk in high risk patients (v 1.2% in CALISTO)

A 67 year old man with cirrhosis, new diagnosis of HCC is admitted with diarrhea, lowish BP and AKI. On exam he has bilateral lower extremity swelling, R> L. In the ED he has an ultrasound which shows thrombosis of the greater saphenous vein extending from the calf proximally and terminating 6 cm from the deep femoral vein. What do you recommend?

a. Prophylactic fondaparinux
b. Prophylactic rivaroxaban
c. Full dose DOAC or warfarin
d. Warm compresses, no anticoagulation
50 year old man presents with unprovoked PE. He is hemodynamically stable but CT PE shows elevated RV/LV ratio. ECHO is ordered. He is admitted and started on rivaroxaban. Should you send a work up for thrombophilia?

- Yes-why not, he is here.
- No-then I am going to have interpret it and who needs that.

No current guidance/guidelines

EXCEPT ASH Choosing Wisely Campaign- “do not test in provoked VTE”

Results of thrombophilia testing should RARELY affect clinical decisions about VTE treatment-no strong influence on recurrence risk beyond stratification based on clinical presentation

Can help explain “why”

Can be of interest to family members

Current tests are insufficient for identifying inherited VTE risk

Who should we suspect harbors thrombophilia?

<table>
<thead>
<tr>
<th>Table 1. Clinical Characteristics Suggestive of Inherited Thrombophilia in Patients with Venous Thromboembolism (VTE).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis at a young age (&lt;50 yr), especially in association with weak provoking factors (minor surgery, combination oral contraceptives, or immobility) or unprovoked VTE</td>
</tr>
<tr>
<td>Strong family history of VTE (first-degree family members affected at a young age)</td>
</tr>
<tr>
<td>Recurrent VTE events, especially at a young age*</td>
</tr>
<tr>
<td>VTE in unusual sites such as splanchnic or cerebral veins†</td>
</tr>
</tbody>
</table>

* The antiphospholipid syndrome must also be considered, but it is not inherited.
† Patients with splanchnic-vein VTE should be assessed for myeloproliferative neoplasms and paroxysmal nocturnal hemoglobinuria.

UNPROVOKED THROMBOSIS IN YOUNG PATIENT THINK ABOUT:

- PROTEIN C, S, ANTITHROMBIN DEFICIENCY OFTEN POSITIVE FAMILY HISTORY
- FACTORY LEIDEN MUTATION AND PROTHROMBIN GENE MUTATION—Northern European descent
- APLS-PRIMARY OR SECONDARY (lupus)
- MAY THURNERS SYNDROME—ILIAC VEIN COMPRESSION SYNDROME...LEFT LOWER EXTREM VENOUS COMPRESSION—LEFT Iliac vein COMPRESSED BY RIGHT Iliac ARTERY
- UPPER EXTREMITY DVT-PAGET SCHROEDERS SYNDROME—THORACIC OUTLET SYNDROME WITH VENOUS COMPRESSION
- NEPHROTIC SYNDROME/IBD/PNH
- PREGNANCY, IVF
- CANCER (less likely < 50 yo)
VENOUS AND ARTERIAL THROMBOSIS

- APLS
- PFO-with paradoxical embolism
- HYPERHOMOCYSTIENEMIA
- SICKLE CELL
- P VERA
- PNH
- HIT
- CANCER
- DIC
- Beurgers disease
- Hyperviscosity-MGUS, MM

Thrombophilia Tests

Table 1: Thrombophilia Tests and Prevalence of Risk Factors

<table>
<thead>
<tr>
<th>Item</th>
<th>Assay</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>Assay</td>
<td>50%</td>
</tr>
<tr>
<td>Factor II/Prothrombin</td>
<td>Assay</td>
<td>10%</td>
</tr>
<tr>
<td>Protein C</td>
<td>Activity assay</td>
<td>50%</td>
</tr>
<tr>
<td>Protein S</td>
<td>Activity assay</td>
<td>50%</td>
</tr>
<tr>
<td>Antithrombin</td>
<td>Activity assay</td>
<td>50%</td>
</tr>
</tbody>
</table>

Summary of Recommendations Regarding Testing for Thrombophilia.

1. Do not test while patient is on anticoagulants
2. Do not test while patient is on heparin
3. Consider testing when positive family history
4. Consider testing when history of recurrent thrombosis
5. Consider testing in pregnant women
6. Consider testing in diabetics
7. Consider testing in smokers
8. Consider testing in patients with a history of deep vein thrombosis
9. Consider testing in patients with a history of pulmonary embolism
10. Consider testing in patients with a history of stroke

Algorithm for Selecting Patients with a First Venous Thromboembolism (VTE) for Thrombophilia Testing.

Splanchnic vein thrombosis
Cerebral vein thrombosis
### Impact of Anticoagulation & Thrombosis on Thrombophilia Labs

<table>
<thead>
<tr>
<th>Protein/C Protein S</th>
<th>Acute Thrombosis</th>
<th>Warfarin</th>
<th>Low Dose Heparin</th>
<th>DOAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein C/Protein S</td>
<td>False Positive</td>
<td>False Positive</td>
<td>No Effect</td>
<td>True Positive, False Normal</td>
</tr>
<tr>
<td>Antithrombin</td>
<td>False Positive</td>
<td>False Positive</td>
<td>False Positive</td>
<td>True Normal</td>
</tr>
<tr>
<td>Lupus Anticoagulant</td>
<td>False Positive</td>
<td>False Positive</td>
<td>False Positive</td>
<td>True Positive, False Normal</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>False Positive</td>
<td>False Positive</td>
<td>False Positive</td>
<td>True Positive, False Normal</td>
</tr>
<tr>
<td>Prothrombin G1 Mutation</td>
<td>False Positive</td>
<td>False Positive</td>
<td>False Positive</td>
<td>True Positive, False Normal</td>
</tr>
</tbody>
</table>

**Reflex Testing:**
- **3-6 months**
- Rarely send APAs acutely if strong suspicion
- CAN SEND ELY/PTG but in heterozygous form

### Antiphospholipid Antibody Syndrome

- **WHY:** risk of recurrence off AC much higher; at risk for arterial disease, bridge therapy; DOACs generally avoided
- **WHO:** arterial and venous events, unexpected arterial events, recurrent thrombosis ON anticoagulation, underlying autoimmune d/o, prolonged aPTT
- **WHAT:** send Lupus anticoagulant, Beta 2 glycoprotein antibodies and anticardiolipin antibodies (IgG & IgM)
- **WHEN:** LAC-don’t do it on anticoagulation; antibodies you can send anytime
- **IF POSITIVE:**
  - Must repeat in 12 weeks-high rate of transient positivity
  - LAC most predictive of 1st and recurrent VTE, triple positives at highest risk

### Thrombophilia Testing

50 year old man presents with unprovoked PE. He is hemodynamically stable but CT PE shows elevated RV/LV ratio. ECHO is ordered. He is admitted and started on rivaroxaban. Should you send a work up for thrombophilia?

- **Yes-why not, he is here.**
- **No-then I am going to have interpret it and who needs that**
What To Do After the Bleed

76 y/o man with CAD (NSTEMI 2006), AFIB CHADS-Vasc=4 on warfarin and ASA is admitted with UGIB. INR is 3.0. He requires 3u PRBCs, vit K and FFP. EGD shows peptic ulcer disease. He is started on high dose PPI therapy, bx for H Pylori done. When should his anticoagulation be restarted?

a) Never
b) In two weeks
c) In three months
d) Let the primary provider deal with this one
"IN THE EVENT OF GI BLEED WE SUGGEST WAITING AT LEAST 7 DAYS WITHOUT EVIDENCE OF ACTIVE BLEEDING AND AFTER ENDOSCOPIC TX BEFORE REINITIATING AC"

GIBs: DOACs vs Warfarin

Resumption of DOACs

Anticoagulation FULLY therapeutic within 1-2 hours

Only dabigatran has a reversal agent

Considerations After GIB on AC

- Reassess risk benefit of anticoagulation secondary prevention of VTE therapy, low CHADS-vasc
- Assess risk of rebleeding from source identifiable source, treatable lesion?
- Take steps to decrease risk of bleeding related to AC regimen
- Reconsider need for antiplatelet therapy if warfarin was INR in range, is control good? spurious elevation in INR or poor TTR → DOAC increase INR monitoring→home POC INR?
- If ongoing strong indication for AC determine best time to restart therapy in multidisciplinary meeting with proceduralist - Remember DOAC immediately active

What To Do After the Bleed

76 y/o man with CAD (NSTEMI 2006), AFIB CHADS-Vasc=4 on warfarin and ASA is admitted with UGIB INR is 3.0. He requires 3u PRBC, vit K and FFP. EGD shows peptic ulcer disease. High dose PPI therapy, bx for H Pylori done. When should his anticoagulation be restarted?

- Never
- In two weeks
- In three months
- Let the primary provider deal with this one

“Two weeks may provide the best balance among GI bleed recurrence, thromboembolism and mortality”

Questions?

Tracy Minichiello, MD
Postoperative Delirium

An 80-year-old woman falls and sustains a hip fracture at her assisted living facility. She has a history of stroke and uses a walker. She has mild dementia. She is alert, oriented to self and place but not date (baseline).

1. How likely is this patient to develop delirium?
2. What can be done to prevent delirium?
3. What should you do if she becomes delirious?

Postoperative Delirium Guideline

American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults:

Clinical Practice Guideline for Postoperative Delirium in Older Adults

Postoperative Delirium in Older Adults: Best Practice Statement from the American Geriatrics Society
http://dx.doi.org/10.1016/j.jamcollsurg.2014.10.019
Postoperative Delirium

Clinical Features:
• Acute, fluctuating disturbance of consciousness
• Reduced ability to focus & attend
• Accompanied by cognitive and perceptual disturbances
• Postop delirium has onset peak 1-3 days after surgery

Usually self-limited but associated with bad outcomes:
• Increased mortality (10-20% rise per 48 hours of delirium)
• Increased LOS, higher risk of institutionalization

Incidence of Delirium

<table>
<thead>
<tr>
<th>Population</th>
<th>Incidence</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-hip fracture</td>
<td>44 - 61% (up to one-third delirious on admission)</td>
<td>Berggren et al. Dolan et al.</td>
</tr>
<tr>
<td>Elective orthopedic</td>
<td>18%</td>
<td>Fisher et al.</td>
</tr>
<tr>
<td>Major elective</td>
<td>9% (46% in aortic surgery)</td>
<td>Marcantonio et al.</td>
</tr>
</tbody>
</table>

Risk Factors (a partial list)

Patient (Chronic) Factors
• Advanced age
• Cognitive impairment
• Functional impairment
• Severe chronic illness
• Substance abuse
• Sensory deficits
• Malnutrition

Acute Factors
• Hip fracture
• Aortic or thoracic surgery
• Fluid / electrolyte disorder
• Sepsis
• Uncontrolled pain
• Polypharmacy
• Anemia
• Kidney injury
• Sleep deprivation

Assessing the Risk of Delirium

AGS guideline recommends preoperative assessment of risk of delirium:
• Consider age > 65, cognitive impairment, sensory deficit, severe illness, and infection
• Validated prediction tools available, but less practical
• For increased risk, would counsel patient & family and consider applying multi-component delirium prevention interventions (if available at your hospital)
Prevention: Care Packages

Multi-component intervention packages:
- e.g., Acute Care for Elderly (ACE) units, Comprehensive Geriatric Assessment (CGA), delirium prevention order sets
- Reorientation, non-drug sleep hygiene, bowel/bladder care, early PT/OT, nutrition, pain assessment, delirium screening
- Moderate evidence for benefit from numerous trials but requires institutional support & group effort

Prevention: Pharmacology

Avoid high-risk medications:
- Anticholinergics, meperidine, BZD & other sedatives
- Minimize opiates by using non-opiate analgesics

Role for prophylactic neuroleptics?
- Several trials of neuroleptics to prevent delirium
- Inconsistent findings, poor study quality
- Bottom line: insufficient evidence for or against

Screening & Diagnosis

- AGS doesn’t take position on whether to screen
- Hyperactive (agitated) delirium usually obvious but hypoactive (sedated) delirium often missed

Confusion Assessment Method (CAM):
1. Acute change or fluctuation in mental status
2. Inattention (trouble focusing or distractible)
3. Disorganized thinking or altered level of consciousness

Evaluating the Delirious Patient

Specific, reversible etiology seldom identified

Approach to working up postoperative delirium:
- CBC, basic chemistry, urinalysis, EKG
- Other studies only if indicated by clinical findings
- Brain imaging rarely useful
- Low yield for thyroid tests, vitamin levels, RPR, LP, etc.

Review medications closely:
- Anticholinergic, BZD, opiate, antiemetic, antispasmodic
Treating Postoperative Delirium

Identify & treat reversible causes:
- Recommended but beware of excessive work-up

Multidisciplinary teams & multicomponent interventions:
- Similar to delirium prevention packages
- Weak & inconclusive evidence for benefit (vs. prevention)

Physical restraints:
- Not recommended unless no other option to prevent harm

Recommendations are based largely on expert opinion:
- Treat specific causes
- Adequate pain control
- Eliminate unnecessary medications, lines, catheters
- Mobilization during daytime
- Quiet, uninterrupted sleep at night
- Frequent re-orientation and reassurance
- Reserve sedation for patients at high risk for self-harm

Morrison RS, et al.  AIM, 1998

Antipsychotics for Management of Postoperative Delirium

Commonly used but poorly studied
- Lack of placebo-controlled trials in postop patients
- Are we changing natural history or just sedating patients?

Indications & Recommendations:
- Only for severe agitation or distress, if threatening substantial harm to self and/or others
- Try behavioral interventions first
- Use lowest effective dose for the shortest possible duration
- Don’t treat hypoactive delirium with antipsychotics


Red Pill, White Pill, Blue Pill
Antipsychotic Regimens for Delirium

Haloperidol:
• Start 0.5 – 1 mg (PO, IV, IM); can repeat in 30-60 min
Risperidal
• Start at 0.5 – 1 mg (PO) BID; peak 1 hr; renal dose
Quetiapine
• Start 25 mg (PO) QHS or BID; peak 1.5 hr
• Preferred for patients with Parkinsonism
Olanzapine
• Start 2.5 mg (PO – also available IV/IM) QHS; peak 6 hr

IV Haldol & Long QTc

• Haldol not approved for IV use, but commonly done
• Risk of QTc prolongation and torsades de pointes
• Risk mainly if ≥ 2 mg single dose or ≥ 20 mg / 24 hrs
• Watch for other drugs that prolong QTc (e.g., methadone)
• UCSF policy:
  -- Tele or daily ECG needed if exceeding above doses
  -- IV haldol held if QTc > 440 ms

Screening for Postoperative MI

Findings from POISE (2008 beta-blocker trial):
• 5% of these “elevated risk” patients had postop MI, defined as elevated biomarker + ECG changes
• Most MI occurred by POD #3 (74% within 48 hr)
• Postoperative MI predicted 5-fold mortality
• Majority of postoperative MI were asymptomatic
• Silent MI had similar mortality as symptomatic MI

Postop Troponin Predicts Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Biomarker</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>POISE (2011)</td>
<td>Troponin or CK-MB</td>
<td>2.5x mortality with isolated biomarker elevation</td>
</tr>
<tr>
<td>VISION (2012)</td>
<td>Troponin-T</td>
<td>4x mortality with any Tn-T elevation</td>
</tr>
<tr>
<td>Meta-analysis of 14 earlier studies (2011)</td>
<td>Troponin</td>
<td>3x mortality with elevation</td>
</tr>
</tbody>
</table>

Arguments Against Screening

Too late to do anything:
- Nearly 2/3 of deaths in patients with MI occurred by POD 3
- Many deaths in MI patients are not cardiac-related
- Elevated troponin just identifies obviously crashing patients

No known effective intervention:
- Don’t order the test unless it will change management

MANAGE Trial

Question: Does the direct thrombin inhibitor dabigatran improve outcomes in patients with elevated postop troponin?

Patients: 1754 patients who evidence of myocardial injury after noncardiac surgery (MINS), defined as elevated postop troponin either with clinical, ECG or imaging evidence of new ischemia or no other explanation (e.g., PE, sepsis, atrial fib)

Intervention: Dabigatran 110 mg bid vs. placebo for up to 2 yrs

Outcome: CV mortality, nonfatal MI, stroke, peripheral arterial thrombosis, and symptomatic PE
- Amputation and symptomatic proximal DVT added post hoc

MANAGE Trial Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dabigatran</th>
<th>Placebo</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary cardiac or vascular outcome</td>
<td>11%</td>
<td>15%</td>
<td>25</td>
</tr>
<tr>
<td>Mortality – CV</td>
<td>6%</td>
<td>7%</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality – All cause</td>
<td>11%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>4%</td>
<td>5%</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>3%</td>
<td>4%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Screening for Myocardial Injury

Limitations of MANAGE trial:
- Design problems (changing sample size & outcomes)
- Outcomes too broad and individually no significant effect
- Comparison group was placebo
- Just too weird – very different from usual practice

So now what?
- Statin & ASA: Association between their use and lower mortality in patients with MINS or postop MI (retrospective study only)
Canadian Cardiovascular Society (CCS)

- Measure BNP or NT-proBNP before major noncardiac surgery in all patients with CV disease, over age 65, or RCRI score > 1
- Use biomarker instead of stress test for risk stratification
- BNP > 92 or NT-proBNP > 300 indicate increased risk
- Measure troponin daily for 48-72 hours after surgery if preoperative biomarker level elevated
- Patients with elevated postoperative troponin should receive long-term aspirin & statin therapy

Delaying Surgery After MI

A 63-year-old man suffers an acute myocardial infarction, treated without PCI. He was already scheduled for prostate cancer surgery in one month.

Because of his recent MI, surgery should be delayed for:

A. 1 month
B. 2 months
C. 3 months
D. 6 months
E. At least a year

Delaying Surgery After Acute MI

**Question:** How does time between acute MI and surgery affect the risk of postoperative MI?

563,842 patients (1999-2004) discharged after hip surgery, colectomy, cholecystectomy, AAA repair, or lower extremity amputation:

- 2.9% of cohort had experienced acute MI in prior year
- Outcome: 30-day postoperative MI

How Long to Wait after MI?

Conclusions:
- Surgery within one year of acute MI associated with high risk of postoperative MI
- Risk falls over time; most of the reduction within 2 months
- Trend is similar when only elective surgery considered

Caveats:
- Nonrandomized, observational study

ACC/AHA Guidelines:
- Delay elective surgery for at least 2 months after MI

Delivering Surgery After Stroke

A 63-year-old man suffers an acute stroke that is managed without thrombolysis. Brain MRI incidentally detects a large meningioma. The neurosurgeon wants to do a craniotomy to resect the tumor in 2 weeks.

Because of his stroke, you recommend delaying surgery for:

A. 1 month  B. 3 months  C. 6 months  D. 9 months  E. At least a year

Question: How does time between stroke and surgery affect the risk of cardiovascular complications?

Danish cohort study of all adults undergoing elective noncardiac surgery from 2005-2011:
- 7137 patients had prior stroke (1.5% of total cohort)
- Outcome: 30-d postop Major Adverse Cardiac Events (MACE): cardiovascular death, nonfatal MI, ischemic stroke
- Looked at effect of time since stroke on MACE rate

Jorgensen ME et al. JAMA 2014; 312:269-277
**How Long to Wait after CVA?**

**Conclusions:**
- Surgery after CVA associated with high CV risk
- Risk falls over 9 months, biggest drop after first 3 months

**Caveats:**
- Nonrandomized, observational study

**My take-away:**
- Delay elective surgery for at least 3 months (up to 9 months) if possible

---

**Perioperative Transfusion Threshold**

82 y.o. woman has undergone repair of a femoral neck fracture. She denies heart disease, but has old pathologic Q-waves on her ECG. On post-op day #2, she only complains of hip pain.

**Examination:**
- BP 140/80
- HR 75
- Heart, Lung, Abdomen exams normal

**Labs:**
- Hemoglobin = 8.3 (Hct = 25%)

*When should she receive a blood transfusion?*

---

**Perioperative Transfusion Threshold**

1. Transfuse to keep Hgb > 10
2. Transfuse to keep Hgb > 9
3. **Transfuse to keep Hgb > 8**
4. Transfuse to keep Hgb > 7
5. Only if symptomatic

---

**FOCUS* Trial**

(*Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair*)

**Patients:**
- 2016 patients undergoing hip fracture repair.
- All patients had either diagnosis of or risk factors for cardiovascular disease.
  - Mean age = 82
  - HTN (82%); CAD (40%); DM (25%); CVA (24%); CHF(17%)

**Treatment:**
- Randomized to 2 transfusion strategies:
  1. Hemoglobin < 10 g/dL
  2. Symptoms of anemia (also permitted for hgb < 8)

FOCUS Trial Results

<table>
<thead>
<tr>
<th></th>
<th>PRBC Units Transfused</th>
<th>Total Units Transfused</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 g/dL Trigger</td>
<td>2 (1,2)</td>
<td>1866</td>
</tr>
<tr>
<td>Symptomatic Trigger</td>
<td>0 (0,1)</td>
<td>652</td>
</tr>
</tbody>
</table>

Carson JL et al. NEJM 2011; 365:2453-62

Conclusion: No increased mortality or morbidity with a restrictive transfusion protocol.

Caveats to FOCUS Trial

- Small difference in hemoglobin levels may not be clinically significant
- Inadequate power to determine if presence of CV disease affects outcome
- Restrictive transfusion strategy leads to more symptomatic anemia (mostly ↑HR or ↓BP)

AABB Transfusion Guidelines

The society formerly known as the American Association of Blood Banks:

- "In postoperative surgical patients, transfusion should be considered at a hemoglobin concentration of 8 g/dL or less or for symptoms (chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure)." **Strong recommendation**
- Same recommendation if patient has pre-existing CV disease **Weak recommendation**

A 65-y.o. man with cirrhosis from HCV desires a hip arthroplasty. He feels well and has no current signs of ascites or encephalopathy on examination.

Labs: Creatinine = 1.6  
Total Bilirubin = 1.9  
Albumin = 3.5  
INR = 1.6

How would you advise this patient about his postoperative mortality risk?

65-y.o. man with cirrhosis from HCV desires a hip arthroplasty. He’s asymptomatic and has no signs of encephalopathy or ascites.

1. Patients with cirrhosis are not candidates for elective surgery
2. Your mild cirrhosis (Childs-Pugh class A) makes you an acceptable surgical candidate
3. Perioperative risk is acceptable, but long-term mortality risk makes surgery unappealing

**Surgical Risk in Cirrhotic Patients**

**Question:** How does his cirrhosis affect mortality risk?

**Background:**

- Risk traditionally assessed by Childs-Pugh classification
  (http://www.mdcalc.com/child-pugh-score-for-cirrhosis-mortality)
- Mortality after GI surgery:
  - Class A = 10%
  - Class B = 30%
  - Class C = 70%
- Limitations: single time point, less known about non-GI surgery; sensitive to minor laboratory result differences

**MELD Score as Risk Predictor**

**MELD Score** (Model for Endstage Liver Disease):

- Main use in organ allocation
- Variables: INR, bilirubin, creatinine

Retrospective multivariate analysis of 772 cirrhotic patients undergoing GI, orthopedic, and CV surgery

- Independent predictors of mortality: Age & MELD Score
- Predicts mortality @ 1 wk, 1 mo, 3 mo, 1 yr, 5 yr


Teh et al. Gastroenterology, 2007
65 y.o. man with stable HCV-related cirrhosis. He has no current signs of encephalopathy or ascites.

Labs: Creatinine = 1.6
Total Bilirubin = 1.9
Albumin = 3.5
INR = 1.6

Childs-Pugh Class A
MELD Score = 19

Mortality Prediction:
- Childs-Pugh: 10% in-hospital mortality
- MELD Score: 6.5% 1 week mortality
  24% 1 month mortality
  36% 3 month mortality
  50% 1 year mortality

OSA & The Surgical Patient

Obstructive Sleep Apnea in Surgical Patients

A 55-y.o. morbidly obese man is scheduled to undergo knee arthroplasty. He has hypertension but no other medical history. He reports occasional fatigue and somnolence. He doesn’t know if he snores or has apneic spells. Exam and recent lab tests are unremarkable.

What should be done?
1. Notify surgical team of suspected OSA
2. Notify surgical team & recommend empiric CPAP postop
3. Delay surgery for formal polysomnography

OSA and the Surgical Patient

OSA probably increases postoperative complications:
- Pulmonary complications (11 of 17 studies)
- Postop atrial fibrillation (5 of 6 studies)

Previously undiagnosed OSA may be associated with more complications than known OSA

Clinical screening tools have high + predictive value

Benefits of positive airway pressure (CPAP, BiPAP) for surgical patients with OSA uncertain

1. Screen patients clinically for OSA risk
   - Snoring
   - Tired or sleepy
   - Observe apnea
   - Pressure (HTN)
   - BMI > 35 kg/m²
   - Age > 50 years
   - Neck > 17” (M)/16” (F)
   - Gender is male

   **STOP-BANG**
   - High risk for OSA if either
     - 5 or more total points
     - 2 STOP points + B, N, or G

   http://www.stopbang.ca/osa/screening.php

2. Patient and care team should be informed about known or suspected OSA

3. Insufficient evidence to recommend delaying surgery to perform advanced testing (polysomnography)
   - Exception: patients with evidence of severe or uncontrolled systemic complications of OSA or impaired gas exchange (e.g., severe pulm HTN, hypoventilation, resting hypoxia)

4. Continue PAP after surgery
   - Insufficient evidence to recommend empiric PAP

---

**Are Curbside Consults Safe?**

You’re happily about to leave the hospital…
…when the orthopedic surgeon calls to say, “My patient’s glucose levels are elevated. She’s otherwise stable. Maybe you could give curbside advice?”

Elevated glucose?
Tell your patient to stop eating.

---

**Are Curbside Consults Safe?**

What’s your personal approach to requests for informal “curbside” advice?

1. I never do curbside consults
2. I ask questions to determine whether curbside is appropriate
3. I’m pretty open to giving curbside advice
Curbside Consults

Studied 47 requests for curbside advice to hospitalist
  • Curbside consultant could ask questions ad lib
  • Made recommendations without seeing patient or chart
  • Different hospitalist performed formal, in-person evaluation

Questions:
  • Did curbside consultant obtain accurate information?
  • Did advice and management differ?

Curbside vs. Formal Medicine Consult

Compared to formal consultation, how often did curbside evaluation lead to:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete clinical information</td>
<td>34%</td>
</tr>
<tr>
<td>Inaccurate clinical information</td>
<td>28%</td>
</tr>
<tr>
<td>Any difference in management</td>
<td>60%</td>
</tr>
<tr>
<td>Major difference in management</td>
<td>36%</td>
</tr>
</tbody>
</table>

Curbside with Caution

Be wary when giving (or requesting) informal advice:
  • Only for basic, generic questions
  • If you’re asking a lot of questions, do a formal consult
  • Avoid in unstable or critically ill patients
  • Offer to perform formal consultation; insist on it if “curbsided” again on same patient
  • Don’t visit patient, write orders, review chart, or submit bill

Thank You

quinny.cheng@ucsf.edu
Point-of-Care Ultrasound (POCUS) is the future of the physical exam

- Questions we’ll address around this topic:
  - What is POCUS for hospitalized patients?
  - Why learn POCUS?
  - How POCUS is used (cases + demo)?
  - How to get started with POCUS (for you & your institution)?

What is POCUS?

- Performed and interpreted by primary provider…
- …at the bedside…
- …to help answer a specific clinical question…
- …quickly
How we use POCUS in Hospital Medicine?
- Diagnostic
- Therapeutic (procedural guidance)
- Treatment monitoring
- Disease screening

Why learn POCUS?
Reason 1: It makes you a better doctor...
- Procedural complications
- Efficiency and accuracy of diagnosis
- Patient satisfaction

Why learn POCUS?
Reason 2: Most IM/HM doctors don’t know much....
(Epecially if you trained awhile ago)

Why learn POCUS?
Reason 3: Despite lack of knowledge, people think its important....

2017 Needs Assessment of UCSF Hospitalists
- 93% I believe POCUS is important for diagnostic purposes in internal medicine.
- 88% I believe POCUS should be a formal part of residency training.
- 93% I believe faculty would benefit from faculty development in POCUS.
Why learn POCUS?

Its coming whether you like it or not...

Cases: Inpatient Care as a POCUS Hospitalist

- Four common inpatient scenarios
  - Brief HPI and exam
  - Demo image acquisition and review normal anatomy/findings
  - Review abnormal images from the case
  - Discuss how POCUS impacted care delivery

Case 1: Mr. Seth is short of breath

- HPI: 61 M wih HF/EF, COPD admitted for COPD exacerbation & CAP.
  - 
    - nebulizers, prednisone, and antibiotics
  - HD #3: increasing respiratory distress and anxiety
  - Vitals: AF, HR 102, BP 192/97, RR 26, O2 sat 82% on RA → 93% on 6L NC
  - Exam:
    - General: moderate distress.
    - CV: Tachycardic, no MRG. Unable to assess JVP. 1+ pitting edema of b/l LEs.
    - Lung: tachypneic, increased WOB, scattered wheeze with bilateral lower lobe rales.
  - Labs: normal CBC and BMP, BNP 421, Trl pending, EKG non-ischemic. CXR ordered.

Case 1: Mr. Seth is short of breath + POCUS!

- On admission, >3 b-lines in R anterior lung, otherwise normal.
- Now, diffuse b-lines in bilateral lung fields, bilateral pleural effusions. IVC 2.4cm and minimally collapsible.

- Vitals: AF, HR 102, BP 192/97, RR 26, O2 sat 82% on RA → 93% on 6L NC
  - Exam:
    - General: moderate distress.
    - CV: Tachycardic, no MRG. Unable to assess JVP. 1+ pitting edema of b/l LEs.
    - Lung: tachypneic, increased WOB, scattered wheeze with bilateral lower lobe rales.
  - Labs: normal CBC and BMP, BNP 421, Trl pending, EKG non-ischemic. CXR ordered.

You were done with your POCUS assessment by the time the CXR was ordered 😊
- **B-lines**
  - Pattern helps you with ddx:
    - Bilateral (interstitial syndrome) vs Focal
    - Higher sensitivity than CXR
    - Useful for dynamic monitoring
Case 1 Resolution

- POCUS diagnosis: interstitial syndrome, pleural effusions, volume overload
- You give him IV Lasix and treat his blood pressure $\rightarrow$ BP normalized and hypoxia improving
- You make a mental note to check his lung and IVC US again tomorrow to decide about thoracentesis and further need for diuretics

Case 1 Take Home Points

- POCUS
  - improved the quality of your index exam
  - helped you quickly identify why his condition acutely changed
- When possible:
  - Have an algorithmic approach
  - Combine multiple pocus exams and integrate with other data
Case 2: Mrs. Essig is hypotensive

- **HPI**: 52W with metastatic breast cancer c/o L malignant pleural effusion on chemotherapy p/w generalized weakness, dyspnea, lethargy, HR 123 BP 82/40
  - Given 2L IVF with improvement.
- **Vitals**: AF, HR 112, BP 90/47, RR 16, O2 sat 96% on RA
- **Exam**:
  - General: arousable but somnolent, comfortable
  - CV: Tachycardic, regular, no MRG. JVP 6cm. Chronic lymphedema of the b/l LEs
  - Lung: breathing comfortably on RA, diminished breath sounds LLB but otherwise CTA bilaterally
- **Labs**: CBC and BMP normal. Tnl 1.6, normal AST/ALT. BNP 235 (unknown baseline). TnI negative.

**POCUS**!
- Cardiac US with mildly reduced LVEF, pericardial effusion
- Lungs with a-line throughout, moderate L pleural effusion
- IVC 1.9cm w/ <30% collapse with inspiration

Demo: Cardiac US (Parasternal Long Axis)

Demo: Cardiac US (Parasternal Short Axis)
**Case 2 Resolution**

- POCUS diagnosis: new mild-moderate LVEF reduction, new small pericardial effusion
- Repeat TTE on HD#1 confirms new EF 40%, pericardial effusion enlarging
- HD#3 she develops tamponade, undergoes pericardial drain placement. Patient and family opt for hospice referral.

**Case 2 Take Home Points**

- POCUS led you to a faster, new diagnosis of HFrEF.
  - Clinical management: more cautious with IVF
  - Further diagnostic testing: ordered TTE from admission
  - Monitoring evolution of pericardial effusion
  - Assist with prognostication & GOC

---

**LV Ejection Fraction**

- **Evaluation**
  - End-point Septal Separation (EPSS)
  - Fractional Shortening
  - Myocardial Thickening

- **Qualitative assessment**
  - Hyperdynamic
  - Normal
  - Mild-moderately reduced
  - Severely reduced

- LV dysfunction by hospitalists: 91% sensitivity, 88% specificity

**Pericardial Effusion**

- **Qualitative assessment**
  - Small
  - Moderate
  - Large

- Pericardial effusion by hospitalists: 100% sensitivity, 87% specificity

- Apical 4 chamber, sub-xiphoid best for evaluating signs of chamber collapse (tamponade)

---

<table>
<thead>
<tr>
<th>Condition</th>
<th>Predictive Value</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Arrest</td>
<td>47/52</td>
<td>84% (95 CI)</td>
<td>71% (95 CI)</td>
<td>2.21</td>
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<tr>
<td>Pericardial effusion, mild</td>
<td>55/45</td>
<td>88% (95 CI)</td>
<td>87% (95 CI)</td>
<td>3.52</td>
<td>0.24</td>
</tr>
<tr>
<td>Pericardial effusion, large</td>
<td>50/50</td>
<td>87% (95 CI)</td>
<td>87% (95 CI)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Case 3: Dr. Nye has an AKI

- **HPI:** 84M with BPH, HTN, DM2 presents with AMS, lower abdominal pain, decreased urination, K 6.4. ED POCUS shows hydronephrosis and a distended bladder
  - → foley with 400cc urine output. hyperK treatment.

- **Vitals:** within normal limits

- **Exam:**
  - General: mildly agitated but redirectable, no distress
  - Abd: soft, suprapubic tenderness, no CVA tenderness, no distension, NABS
  - GU: foley in place draining cloudy yellow urine

- ** Labs:** WBC 11.7, BUN 48, Cr 2.6, K 6.1, otherwise normal. UA +WBC, +nitrite, +LE, +Blood. Urine culture pending. CTAP pending.

Demo: Renal Ultrasound (LUQ)
Hydronephrosis
- Arises from renal pelvis and extends through kidney
- Grading:
  - Mild-moderate
  - Severe

Bladder Volume
- Measure in transverse and longitudinal planes
- \( L \times W \times H \times 0.5 \)

Case 3 Resolution
- POCUS diagnosis: severe hydronephrosis, foley dysfunction with urinary retention
  - Foley is flushed and repositioned \( \rightarrow \) additional 800cc urine output. He is started on ceftriaxone for UTI and Tamsulosin for BPH. His abdominal pain resolves; you cancel the CT scan.
  - HD #2: urine culture + for pan-sensitive E.Coli \( \rightarrow \) abx narrowed to cephalexin. K, Cr improved. Foley is removed and he passes a trial of void prior to discharge.
Case 3 Take Home Points

- POCUS helped you quickly identify a complication in your treatment plan
  - → avoided a potential bad outcome & unnecessary CT scan.
- Accuracy of bladder volume by POCUS > bladder scan
- Detecting hydronephrosis is a readily attainable skill
  - IM residents x5 hrs of renal US practice = 94% sensitivity; 93% specificity for moderate-severe hydronephrosis

Case 4: Ms. Nidus has cellulitis

- HPI: 36W with IVDU, DVT not on anticoagulation presents Saturday night with a red, swollen, and painful RLE. No fevers or chills.
  - → IVF, empiric antibiotics for cellulitis and orders a RLE Doppler
- Vitals: Afebrile, HR 98, BP 108/55, RR 16, O2 sat 98% RA
- Exam:
  - General: awake, alert, cooperative. In mild distress 2/2 pain.
  - CV: RRR, no MRG.
  - MSK: RLE tender, erythematous, warm to touch distally. No fluctuance or purulence. She is diffusely TTP overlying the area. Mild pitting edema of R>LLE. Intact pulses.
- Labs: WBC 12.3, CBC otherwise normal. CMP normal. Lactate 2.1. D-dimer 785. Doppler RLE is ordered, but won’t be performed until the techs arrive on Monday morning.

How many people would anticoagulate her? 

Case 4: Ms. Nidus has cellulitis + POCUS!

- IVF, empiric antibiotics for cellulitis and orders a RLE Doppler
- Vitals: Afebrile, HR 98, BP 108/55, RR 16, O2 sat 98% RA
- Exam:
  - General: awake, alert, cooperative. In mild distress 2/2 pain.
  - CV: RRR, no MRG.
  - MSK: RLE tender, erythematous, warm to touch distally. No fluctuance or purulence. She is diffusely TTP overlying the area. Mild pitting edema of R>LLE. Intact pulses.
- Labs: WBC 12.3, CBC otherwise normal. CMP normal. Lactate 2.1. D-dimer 785. Doppler RLE is ordered, but won’t be performed until the techs arrive on Monday morning.

Demo: Soft Tissue Ultrasound
- SSTI
  - Cobblestoning (cellulitis)
  - Deep fluid pocket (abscess)
  - Hospitalists ID’ing abscess: 97% sensitivity, 84% specificity

DVT US
- Compression-only
- 5 branch points (including popliteal)
  - Sensitivity 100%
  - Specificity 99%
  - Compared to radiology

Case 4 Resolution
- POCUS diagnosis: cellulitis, no abscess, +/- DVT. Safe for further fluid resuscitation.
- You give an additional 1L IVF → lactate, BP normalizes
- You start her on therapeutic lovenox for DVT seen on POCUS; confirmed by radiology DVT study 36 hours later.
- She tolerates oral antibiotics well, cellulitis improves. Prior to discharge, switch to oral DOAC with plans to follow up with a community PCP
Case 4 Take Home Points

- In a resource-limited environment (overnights, weekends) POCUS can lead to faster initiation of appropriate therapy
- POCUS can help guide fluid resuscitation in the setting of hypotension or tachycardia.
- Just because you POCUS, doesn’t mean you can’t order the formal study!

So why do we POCUS?

- Earlier diagnosis and treatment
- Avoids additional tests and reduces radiation exposure
- Safe treatment monitoring, prognostication
- Skills are attainable and lead to better quality care delivery than exam alone

POCUS doesn’t replace the physical exam; it enhances the physical exam.

It IS the physical exam

Data for the POCUS we covered

<table>
<thead>
<tr>
<th>Exam</th>
<th>Statistical Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC</td>
<td>Correlation coefficient 0.7-0.9</td>
</tr>
<tr>
<td>LVEF</td>
<td>LR +5.4; LR -0.2</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>LR +7.7; LR -0.0</td>
</tr>
<tr>
<td>Pulmonary Edema</td>
<td>Sensitivity 94%; Specificity 92%</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>Sensitivity 95%; Specificity 96%</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>Sensitivity 94%; Specificity 93%</td>
</tr>
<tr>
<td>DVT</td>
<td>Sensitivity 100%; Specificity 98%</td>
</tr>
<tr>
<td>Abscess</td>
<td>Sensitivity 97%; Specificity 84%</td>
</tr>
</tbody>
</table>

Data for POCUS Algorithms

- Rapid Ultrasound in Shock and Hypotension (RUSH)

<table>
<thead>
<tr>
<th>Findings Diagnosis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A lines (normal)</td>
<td>Asthma/COPD</td>
<td>89</td>
</tr>
<tr>
<td>Diffuse B lines (&gt;2 lung zones)</td>
<td>Pulmonary edema</td>
<td>97</td>
</tr>
<tr>
<td>Loss of pleural line, consolidation, patchy B lines</td>
<td>Pneumonia</td>
<td>89</td>
</tr>
<tr>
<td>Abscess</td>
<td>Sensitivity 97%; Specificity 84%</td>
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</tbody>
</table>

- BLUE protocol for dyspnea/hypoxia

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<th>Diagnosis</th>
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<td>Sensitivity 97%; Specificity 84%</td>
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<td></td>
</tr>
</tbody>
</table>
What is the scope of POCUS in HM?

How should you integrate POCUS into your practice?

- Many factors to think through:
  - Context
  - Frequency
  - Difficulty
  - Data

Scope of POCUS in HM at UCSF

Addressing Barriers

- Hardware
- Training
- Time and money constraints
- Credentialing and privileging
POCUS Learning Pathways

- Pursue a certificate program (SHM, CHEST)
- Attend workshops (SHM, ACP, AIUM, UCSF)
- Learn from local experts (EM, critical care colleagues)
- Self-learning, ad hoc (FOAMed)

Our institution’s experience

Getting started...

- Champion(s)
- Leadership buy-in
  - Education
  - Research
  - Cost savings
  - Clinical outcomes

Building momentum...

- Training program development
- Equipment investment

Making it official

1. Privileging and Credentialing
2. Quality assurance
3. Integration into EMR and billing

Notary stamp?
"The larger issue now is to decide whether we believe that – in this case hospitalists – building competency in ultrasound among generalist physicians will enhance patient safety, quality, and value. Personally, I do."

- Bob Wachter, 2012

Review of Session Goals

- What is POCUS for hospitalized patients?
- Why learn POCUS?
- How POCUS is used (cases + demo)?
- How to get started with POCUS (for you & your institution)?

POCUS is the future of the physical exam.

Questions?

- Trevor.Jensen@ucsf.edu
NOTES
Diagnosis and Management of Acute Kidney Injury

23rd Annual Management of the Hospitalized Patient

Lowell Lo, MD
Associate Clinical Professor
Renal Ambulatory Service and Practice Chief
Mount Zion Dialysis Unit Medical Director
Division of Nephrology
University of California San Francisco

Disclosure

There are no conflicts of interest to disclose.

My Boss’s Boss Instruction

Thou shalt “have a good sense of what the audience need to know about diagnosing and managing inpatients with rising creatinine”

Objectives

- Differentiate scenarios that may not be JUST acute tubular necrosis (ATN)
- Explain the limitation of common lab tests
- Devise a treatment plan for non-oligouric ATN
Overview

- The pre, post, and “intrinsic” (15 mins)
- The patient’s Cr bumped (45 mins)
- Will the patient need dialysis (5 mins)
- Will the patient recover (5 mins)
- Covid-19 and kidney injury (5 mins)

A Word about ARF to AKI

“The diagnosis of ‘injury’, by contrast, does not presuppose a reduction in glomerular filtration...The analogy to cardiology may be instructive: clinicians diagnosing acute myocardial infarction do not wait until a reduction in cardiac output, but rather make the diagnosis of myocardial injury on the basis of elevations of tissue-specific biomarkers in the serum.”

WalkerCurr Opin Nephrol Hypertens 2007

Cr Bump – 3 Variations

Objectives

- Differentiate scenarios that may not be JUST acute tubular necrosis (ATN)
- Explain the limitation of common lab tests
- Devise treatment plan for non-oligouric ATN
Case 1 (ARS)

- 52 y/o male with PMH of poorly controlled T2DM over 10 years, HTN over 15 years, ongoing tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 admitted for non-healing foot ulcer and possible osteomyelitis of the toes. He was started on IV vanc and PO cipro. On day 4 of admission, he became altered and his SBP dropped to 80s (baseline 130s on Losartan, Amlodipine, and Carvedilol). He received 2L of LR and was urgently operated with toe amputation. On day 5, his Cr increased to 2.5 and received 2 more liter of LR. On day 6, his Cr increased to 2.8 and surgical bone Cx grew mixed GPC and GNR. On day 7, his Cr increased to 3.6 and nephrology was consulted. What’s the cause of his AKI?

A: Pre-renal
B: Acute tubular necrosis
C: Acute interstitial nephritis
D: Post-renal

A Wise Nephrologist Once Told Me:

“If you fell asleep during Nephrology Clerkship and woke up by the dreaded question of why did this patient have renal failure, just say ATN”

Case 1 (ARS with answer)

- 52 y/o male with PMH of poorly controlled T2DM over 10 years, HTN over 15 years, ongoing tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 admitted for non-healing foot ulcer and possible osteomyelitis of the toes. He was started on IV vanc and PO cipro. On day 4 of admission, he became altered and his SBP dropped to 80s (baseline 130s on Losartan, Amlodipine, and Carvedilol). He received 2L of LR and was urgently operated with toe amputation. On day 5, his Cr increased to 2.5 and received 2 more liter of LR. On day 6, his Cr increased to 2.8 and surgical bone Cx grew mixed GPC and GNR. On day 7, his Cr increased to 3.6 and nephrology was consulted. What’s the cause of his AKI?

A: Pre-renal
B: Acute tubular necrosis
C: Acute interstitial nephritis
D: Post-renal

A Wise Nephrologist Once Told Me:

“A Nephrologist is an Internist who spins the urine.”
Case 1

- 52 y/o male with PMH of poorly controlled T2DM over 10 years, HTN over 15 years, ongoing tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 consulted for AKI with Cr increased to 3.6. Urine microscopy showed:

Case 1 - “Intrinsic”

1. Proximal Cell becomes apical blebs
2. Loss of the brush border membrane
3. Loss of polarity and integrity of the tight junctions (Back-Leak)
4. Sloughing of live and dead cells, cast formation and obstruction of the tubular lumen

Case 1 – What is ATN

- 52 y/o male with PMH T2DM, HTN, tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 consulted for AKI. Cr increased to 3.6 on day 7 with urine microscopy showed + muddy brown casts. A diagnosis of ATN secondary to osteomyelitis from mixed GPC and GNR was made. Vancomycin and cipro was continued. His Cr peaked on day 9 at 4.3. On day 10, his Cr down trended to 3.9 and his Cx grew MSSA (vanc changed to nafcillin) and GNR grew pseudomonas sensitive to cipro (continued). On day 11, his Cr further improved to 3.2 (renal team signed off). As the team was planning to discharge the patient on day 13 to SNF, his AM lab showed Cr increased from 2.5 back to 3.5. What’s the cause of the new AKI?

- A: Pre-renal
- B: Acute tubular necrosis
- C: Acute interstitial nephritis
- D: Post-renal

Case 1 – Continue (ARS)

- 52 y/o male with PMH T2DM, HTN, tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 consulted for AKI. Cr increased to 3.6 on day 7 with urine microscopy showed + muddy brown casts. A diagnosis of ATN secondary to osteomyelitis from mixed GPC and GNR was made. Vancomycin and cipro was continued. His Cr peaked on day 9 at 4.3. On day 10, his Cr down trended to 3.9 and his Cx grew MSSA (vanc changed to nafcillin) and GNR grew pseudomonas sensitive to cipro (continued). On day 11, his Cr further improved to 3.2 (renal team signed off). As the team was planning to discharge the patient on day 13 to SNF, his AM lab showed Cr increased from 2.5 back to 3.5. What’s the cause of the new AKI?
Case 1 – Continue

• New urinary sediment reviewed:

![Urine Sediment Images]

Case 1 – Continue (ARS with answer)

• 52 y/o male with P1MN T2DM, HTN, tobacco use, PVD, and CKD stage 3b with baseline ~Cr 1.9 consulted for AKI. Cr increased to 3.6 on day 7 with urine microscopy showed + muddy brown casts. A diagnosis of ATN secondary to osteomyelitis from mixed GPC and GNR was made. Vancomycin and cipro was continued. His Cr peaked on day 9 at 4.3. On day 10, his Cr down trended to 3.9 and his Cx grew MSSA (vanc changed to nafcillin) and GNR grew pseudomonas sensitive to cipro (continued). On day 11, his Cr further improved to 3.2 (renal team signed off). As the team was planning to discharge the patient on day 13 to SNF, his AM lab showed Cr increased from 2.5 back to 3.5. What’s the cause of the new AKI?

A: Pre-renal
B: Acute tubular necrosis
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D: Post-renal

Case 1 – AIN

• Clinical suspicion
• Onset s/p potential culprit meds (1-2 weeks with new exposure or few days with repeated exposure)
• Pyuria (50-90%), tubular proteinuria
• Fever, rash (15-50%)
• Eosinophilia

Case 1 - Urine Eosinophil Testing?

“At 1% cutoff, the test does not shift pretest probability of AIN in any direction.”
“Even at 5% cutoff, UEs performed poorly in distinguishing AIN from ATN or other kidney diseases.”

Perazella Clinical Nephrology 2014

Muriithi CJASN 2013
Case 1 – End

The patient was diagnosed with presumptive AIN secondary to Cipro (The patient had multiple exposures to penicillin like Augmentin prior). Despite stopping cipro, his creatinine continued to increase. He received a renal biopsy which confirmed AIN. Then he was treated with prednisone for a month with Cr eventually settled in the high 2s after 6 months.

Case 1 – My Pearls for AKI NOT? ATN

- No major medical events – unexplained Cr rise
- Patients appear well with great/graduate Cr rise
- Positive hematuria and proteinuria (always get an UA before renal consult if possible)
- Pyuria with negative Culture
- Inpatient de novo GN (except for infectious GN) is very rare

- No muddy brown cast ≠ no ATN
- Patients can have AIN without urinary WBCs

Overview

- The pre, post, and "intrinsic" (15 mins)
- The patient's Cr bumped (45 mins)
- Will the patient need dialysis (5 mins)
- Will the patient recover (5 mins)
- Covid-19 and kidney injury (5 mins)

Case 2

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and shortness of breath. On DOA, the patient had CT PE protocol which ruled out PE and PNA. On day 2, she had RHC which showed elevated right (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. She was diagnosed with decompensated heart failure and started on IV Lasix but did not make much urine. Her Cr trend:
Case 2 (ARS)

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and shortness of breath. On DOA, the patient had CT PE protocol which ruled out PE and PNA. On day 2, she had RHC which showed elevated right- (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. She was diagnosed with decompensated CHF and started on IV Lasix but only made about 1L of urine. Cr increased from 1.1 to 1.5 to 2 to 2.9. Nephrology was consulted for whether to continue diuresis. What was the cause of the patient’s AKI?

A: Pre-renal  
B: Acute tubular necrosis  
C: Acute interstitial nephritis  
D: Post-renal

Case 2 (ARS with answer)

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and shortness of breath. The patient was s/p CT PE protocol on DOA which ruled out PE and PNA. On day 2, she had RHC which showed elevated right- (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. She was diagnosed with decompensated CHF and started on IV Lasix but only made about 1L of urine. Cr increased from 1.1 to 1.5 to 2 to 2.9. Nephrology was consulted for whether to continue diuresis. What was the cause of the patient’s AKI?

A: Pre-renal  
B: Acute tubular necrosis 2/2 contrast nephropathy  
C: Acute interstitial nephritis  
D: Post-renal

Case 2 (ARS)

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and decompensated heart failure exacerbation. Her hospital course was complicated by contrast nephropathy. Assuming her baseline GFR was normal at 100mL/min and her creatinine peaked at close to 4 and level off. What was her GFR at the arrow point?

A: ~100mL/min  
B: ~80mL/min  
C: ~50mL/min  
D: ~20mL/min

Case 2 (ARS with answer)

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and shortness of breath. The patient was s/p CT PE protocol on DOA which ruled out PE and PNA. On day 2, she had RHC which showed elevated right- (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. She was diagnosed with decompensated CHF and started on IV Lasix but only made about 1L of urine. Cr increased from 1.1 to 1.5 to 2 to 2.9. Nephrology was consulted for whether to continue diuresis. What was the cause of the patient’s AKI?

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D: Post-renal

Objectives

- Differentiate scenarios that may not be JUST acute tubular necrosis (ATN)

- Explain the limitation of common lab tests

- Devise a treatment plan for non-oligouric ATN
Case 2 – Assessing Kidney Fx in AKI

- Limitations of serum [Cr]
  - Not helpful when not in steady state

The patient’s kidney function has been the same since day 1 of injury. Clinical implication would be dosing medications with GFR < 10-30mL/min and avoid meds that will accumulate in patients with advanced kidney disease.

Case 2 (ARS with answer)

- 85 y/o female with PMH of aflutter, T2DM and HTN presenting with Afib RVR and decompensated heart failure exacerbation. Her hospital course was complicated by contrast nephropathy. Assuming her baseline GFR was normal at 100mL/min and her creatinine peaked at close to 4 and level off. What was her GFR at the arrow point?

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D: ~20mL/min

Case 2 (ARS)

- 85 y/o female with PMH of aflutter, T2DM and HTN presenting with Afib RVR and decompensated heart failure exacerbation. Her RHC showed elevated right (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. However, creatinine continued to increase with diuresis. Should we continue diuresis?

A: Yes
B: No, waitful watching
C: No, check FeNa
D: No, check FeUrea
E: No, give IVF
Case 2 – Lasix vs IVF

- Limitations of FeNa
  - Not helpful when not Oligouric

- Purpose of FeNa: Explain why a patient is oliguric

- If a patient is not oliguric, what does FE_{Na} represent?

- Assuming normal renal function, what would your FE_{Na} be?

---

Case 2 – Origin of FeNa

**Fractional Excretion of Sodium**

*Exceptions to Its Diagnostic Value*

Stuart Zarich, MD; Leslie S. T. Fang, MD, PhD; Jonathan R. Diamond, MD

- Low FE_{Na} reported in:
  - Oliguric ATN
  - CIN
  - Acute glomerulonephritis
  - Myoglobin-induced AKI

- FE_{urea} better if diuretics involved

- Unclear whether studies included CKD

---

A Wise Nephrologist Once Told Me:

"Acute tubular necrosis is a solute retention state."

---

Case 2 (ARS with answer)

- 85 y/o female with PMH of aflutter, T2DM and HTN presenting with Afib RVR and decompensated heart failure exacerbation. The patient developed contrast nephropathy. Her RHC showed elevated right (Mean RA ~31 mmHg) and left-sided (PCWP ~33 mmHg) filling pressures with low CO. However, creatinine continued to increase with diuresis. Should we continue diuresis?

A: Yes
B: No, waitful watching
C: No, check FeNa
D: No, check FeUrea
E: No, give IVF
Case 2 – Assessment and Plan

- 85 y/o female with PMH of atrial flutter, T2DM and HTN presenting with Afib RVR and decompensated heart failure exacerbation. The patient developed contrast nephropathy. Her RHC showed volume overload. She was managed with IV Lasix with minimal response and transitioned to inotrope infusion and IV bumex gtt. Her creatinine continued to worsen daily.

- What can a nephrologist do that an internist can’t do now?

- Intensive Insulin Therapy
- Loop Diuretics
- Erythropoietin
- Insulin-like growth factor
- Thyroxine
- Dopamine
- Fenoldopam

Case 2 – Nephrologist = Internist PLUS

Objectives

- Differentiate scenarios that may not be JUST acute tubular necrosis (ATN)
- Explain the limitation of common lab tests
- Devise a treatment plan for non-oligouric ATN

Plan: FEN

- 1) Solute/Fluid
- 2) Na
- 3) K
- 4) HCO3/AG
- 5) Ca/Mg/Phos
- 6) BUN/Nutrition/Uremia
Case 2 – Assessment and Plan

**Plan:** FEN

- 1) Solute/Fluid
- 2) Na
- 3) K
- 4) HCO₃/AG
- 5) Ca/Mg/Phos
- 6) BUN/Nutrition/Uremia

**S:** + SOB, fatigue, poor appetite, +N and small amount of V

**O:** AF, HR 80s, RR 16, BP 90/50, O₂ Sat 97% on 4LNC, Wt 72.6 (Adm 71.6), Intake 430mL UOP 800mL

**PE:** JVD to mandible, irregularly irregular, bibasilar crackles, Bilateral †+ thigh edema, + asterixis

**Case Profile**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>122</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.9</td>
</tr>
<tr>
<td>HCO₃</td>
<td>18/12</td>
</tr>
<tr>
<td>Ca</td>
<td>7.8</td>
</tr>
<tr>
<td>Mg</td>
<td>2.5</td>
</tr>
<tr>
<td>Phos</td>
<td>5.1</td>
</tr>
</tbody>
</table>

**Case 2 – Assessment and Plan**

1) **Solute/Fluid** (Wt ~5Kg + up) – Total solute overload, perfusion pressure OK

   - Increase bumex gtt and low sodium diet

2) **Na** (122) – Total water overload

   - Fluid restriction to < 1L per day

3) **K** (4.9) – Total body K adequate

4) **HCO₃/AG** (18/12) – likely NAGMA due to decreased ammoniagenesis and dilutional

   - May improve with diuresis

5) **Ca/Mg/Phos** (7.8/2.5/5.2) – Mild hypoCa from resistance to PTH and decreased 1,25-OH vitamin D and hyperMg/hyperPhos from decreased excretion

   - Renal diet to decrease phos intake (not too concerned right now given poor PO intake)

6) **BUN/Nutrition/Uremia** (79) – Concerning with decreased PO intake, +N/V, + asterixis

   - Patient is needing dialysis soon if renal function doesn’t start to recover (hoping for renal recovery by 7-10 days with CIN).

   - Dialysis indication – uremia *don’t let BUN level lead you around by the nose

**Case 2 – My Pearls for BUN level**

- **[C] = m/K**, concentration = mass production rate/clearance

  (in medicine, you can substitute clearance with renal function)

- **Elevated BUN states without uremia**
  - Excessive protein feeding (ex: transitioning off CVVHD to IHD)
  - GI Bleed
  - High catabolic state (ex: high dose steroid)

- **Low BUN states with uremia**
  - Malnourished state
Case 2 – One more word about BUN

• BUN is not a true uremic toxin – it is a SURROGATE

<table>
<thead>
<tr>
<th>System Group</th>
<th>Example</th>
<th>Source</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptide and small proteins</td>
<td>Beta, microglobulin</td>
<td>Shed from RBCs</td>
<td>Pouch-shaped due to large size</td>
</tr>
<tr>
<td>Guanidines</td>
<td>Guanidinoacetic acid</td>
<td>Arginine</td>
<td>Increased production in uremia</td>
</tr>
<tr>
<td>Phosphates</td>
<td>p-Cresol sulfate</td>
<td>Phenylalanine, tyrosine</td>
<td>Protein bound, produced by gut bacteria</td>
</tr>
<tr>
<td>Amines</td>
<td>Indicatine</td>
<td>Tyrosine</td>
<td>Protein bound, produced by gut bacteria</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Arginine</td>
<td>Glutamine</td>
<td>Large volume of distribution, produced by gut bacteria</td>
</tr>
<tr>
<td>Nucleotides</td>
<td>Nucleoside</td>
<td>RNA</td>
<td>Most prominent of all DNA and RNA</td>
</tr>
<tr>
<td>Citrate acids</td>
<td>Oxalate</td>
<td>Acetic acid</td>
<td>Formation of crystal deposits</td>
</tr>
<tr>
<td>Carboxylics</td>
<td>Urocosil</td>
<td>Glycolic intermediates</td>
<td>React with protein to form advanced glycation-end products</td>
</tr>
</tbody>
</table>

Meyer NEJM 2007

Case 2 – End

• 85 y/o female with PMH of aflutter, T2DM and HTN presenting with A5b RVR and decompensated heart failure exacerbation. The patient developed contrast nephropathy. After 2 days of high dose bumex gtt and inotrope, the patient’s UOP increased to 3L per day with Cr slightly down trending. The next day, despite reducing bumex gtt to spot dosing, she made 5L UOP with Cr down to low 3s with resolution of N/V and asterixis.

Case 2 – Reflection

• Did I do anything to help with this case?

  -- I diagnosed the patient with contrast nephropathy

  -- I reassured the team that despite Cr going up, it was ok to continue diuresis

  -- I helped keeping an eye on FEN and got ready to perform dialysis while being hopeful for the potential renal recovery around 7-10 days

Case 2 – My Pearls for CIN Prophylaxis

• IV saline, IV saline, IV saline
• How much?
  - Enough that pt doesn’t develop shortness of breath
  - 100cc/hr x3-6hrs pre and 6-12hrs post
  - NO pre-emptive dialysis
  - NO IV NaHCO3
  - NO mucomyst

Weisbord NEJM 2018, Brar Lancet 2014
Case 3

- 90 y/o male with PMH of HFpEF, afib s/p pacemaker, COPD, CKD baseline Cr ~2, T2DM and BPH admitted for worsening cough, shortness of breath and orthopnea. He was diagnosed with CHF exacerbation and diuresed ~2L the first 2 days. Cr on admission was close to baseline, worsened initially and improved back to baseline after diuresis. The AM prior to consultation he went into Afib RVR. The day of consultation his Cr rose from 2 → 2.46. The team consulted us to assist with AKI management specifically regarding whether to give Lasix or IVF.

Case 3 (ARS)

- After his episode of Afib with RVR s/p amiodarone load, the patient developed hypercapnic respiratory failure with pH 7.15, CO2 78, O2 66 → ICU and intubated. Post intubation, the patient developed shock requiring 1L NS bolus followed by initiation of norepinephrine. On exam, the patient’s SBP was 110s and HR 70s. Pertinent exam: Afib, rate controlled, + JVD without peripheral edema, decreased BS at bases, and extremities are warm. His TTE showed severe tricuspid regurgitation, LV ejection fraction was estimated to be 45 to 50%. Mechanical ventilation precluded the accurate estimation of right atrial pressure. CXR showed worsening of perihilar opacity which may reflect edema, infection, or acute lung injury, with moderate layering effusions. CT chest non-con showed dependent consolidation throughout the mid to lower lungs suspicious for aspiration, infection, or dependent edema and esophageal pathology that predisposed to aspiration. The patient became +1.5L with only 190mL UOP through the day. Renal was consulted for management of AKI and volume status. We should recommend:
  A: Bolus IVF for septic shock
  B: Give IV loop diuretics for ATN
  C: Start patient on CVVHD

A Wise Nephrologist Once Told Me:

“If you don’t know what to do with the fluid status, consult nephrology.”

Case 3 – My Pearl for ATN Fluid Management

Lasix vs IVF?

- The patient’s total solute is UP (from ATN) and renal injury already occurred (from aspiration + Afib c RVR)
- The million-dollar question is: Will perfusing pressure improve with off-loading vs additional loading solute during mixed shock?

My Approach:

- Give liters of base containing IVF during frank septic/hemorrhagic shock, sepsis (especially abdominal), and hepatorenal (give albumin)
- It is much easier to put solute in than taking out during ATN
- When not so certain, give diuretic aiming even to slightly negative fluid balance (ATN is a solute retention state)
- ARDS net trial – aggressive diuresis after initial IVF reduces ICU length of stay
- Need to be even more careful with IVF when patient is oligoanuric despite high dose loop diuretic (should involve renal in these cases)
Case 3 (ARS with answer)

- After his episode of Afib with RVR s/p amiodarone load, the patient developed hypercapnic respiratory failure with pH 7.15, CO2 78, O2 66 → ICU and intubated. Post intubation, the patient developed shock requiring 1L NS bolus followed by initiation of norepi gtt. On exam, the patient’s SBP was 110s and HR 70s. Pertinent exam: Afib, rate controlled, + JVD without peripheral edema, decreased BS at bases, and extremities are warm. His TTE showed severe tricuspid regurgitation. LV ejection fraction was estimated to be 45 to 50%. Mechanical ventilation precluded the accurate estimation of right atrial pressure. CT chest non-con showed dependent consolidation throughout the mid to lower lungs suspicious for aspiration, infection, or dependent edema and esophageal pathology that predisposed to aspiration. The patient became +1.5L with only 190mL UOP through the day. Renal was consulted for management of AKI and volume status. We should recommend:

A: Bolus IVF for septic shock  
B: Give IV loop diuretics for ATN  
C: Start patient on CVVHD

---

Case 3 – Assessment and Plan

**Events:** s/p IV diuril+bumex, IV Abx and off pressor with improved oxygenation

**S: intubated**  
O: AF, HR 70s, RR 16, BP 154/76, O2 Sat 98% on 40%FiO2, Wt 73.5 (Adm 81.6), Intake 1.3L UOP 1.7L  
PE: JVD elevated, +crackle at bases, no dependent edema, alert following command

**Plan: FEN**

1) **Solute/Fluid**
2) **Na**
3) **K**
4) **HCO3/AG**
5) **Ca/Mg/Phos**
6) **BUN/Nutrition/Uremia**

---

Case 3 – Assessment and Plan

1) **Solute/Fluid** – Total solute still up with pulm edema, perfusion pressure fine  
   Continue IV diuril and bumex

2) **Na (149)** – Water deficient (WHAT? Should I give diuretics?)
   **What to do??**

3) **K (4)** – Total body K adequate for now, monitor for hypoK
4) **HCO3/AG (22/20)** – Met Alkalosis (from diuretics) and Gap acidosis (from ATN)
5) **Ca/Mg/Phos (9/2.3/6.2)** – HyperPhos from decreased excretion

Renal diet +/- phos binder pending on trend
6) **BUN/Nutrition/Uremia (132)** – Uremia? Dialysis?

---

Case 3 (ARS)

- Patient is hypertensive, + pulm edema and + hypernatremia. How to manage the patient?

A: Continue IV diuril and bumex for volume overload
B: Waitful watching
C: Only give diuril and stop IV bumex to generate hyponatremia
D: Continue IV diuril and bumex and give NGT water 500cc q4hr
E: Stop IV diuril and bumex and give NGT water 500cc q4hr
**Case 3 – Volume Expansion And Dehydration**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Admission Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Water (L)</td>
<td>40</td>
<td>43</td>
<td>42.2</td>
<td>41.8</td>
<td>41.6</td>
<td>7.6</td>
</tr>
<tr>
<td>[Na] (meq/L)</td>
<td>140</td>
<td>140</td>
<td>140</td>
<td>142</td>
<td>145</td>
<td>146</td>
</tr>
<tr>
<td>Net Water Balance (L)</td>
<td>+0.8</td>
<td>0.8</td>
<td>0.5</td>
<td>0.5</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Overview**

- The pre, post, and “intrinsic” (15 mins)
- The patient's Cr bumped, what now (45 mins)
- **Will the patient need dialysis (5 mins)**
- Will the patient recover (5 mins)
- Covid-19 and kidney injury (5 mins)

**A Wise Nephrologist Once Told Me:**

“The rules of A, E, I, O, U are not helpful to a Nephrologist.”

**Case 3 (ARS with answer)**

- **Patient is hypertensive, + pulm edema and + hypernatremia. How to manage the patient?**
  - A: Continue IV diuril and bumex for volume overload
  - B: Waitful watching
  - C: Only give diuril and stop IV bumex to generate hyponatremia
  - D: **Continue IV diuril and bumex and give NGT water 500cc q4hr**
  - E: Stop IV diuril and bumex and give NGT water 500cc q4hr

**A Wise Nephrologist Once Told Me:**

“The rules of A, E, I, O, U are not helpful to a Nephrologist.”
Case 3 – My Pearls for Dialysis Need

- **BUN/Nutrition/Uremia (132)** – Uremia? Dialysis?

1. Acidosis, Electrolytes, Overload
   -- oligo-anuria without hope of renal recovery soon

2. Ingestion
   -- depends on renal function, level, and type of toxin

3. Uremia
   -- AMS (diagnosis of exclusion)
   -- cardiac rub
   -- poor nutritional intake, N/V

---

Case 3 – Any Outcome Diff with early HD

The patient received IV bumex and 2.5L FW via NGT. His respiratory status improved leading to successful extubation the next day. The patient’s FEN parameters all started to improve.

- **Up to 20% of all admissions**
- Independently associated with increased:
  - Inpatient mortality
  - Length of stay
  - Hospital costs
- Rise in serum Cr of ≥0.5 mg/dL:
  - 6.5-fold increase in odds of death
  - 3.5-day increase in LOS
  - $7,500 in excess hospital costs

References:
Zeng JASN 2014; Chertow JASN 2005
Overview

- The pre, post, and “intrinsic” (15 mins)
- The patient’s Cr bumped, what now (45 mins)
- Will the patient need dialysis (5 mins)
- Will the patient recover (5 mins)
- Covid-19 and kidney injury (5 mins)

Case 4

- 42 y/o male with PMH of HTN and obesity admitted for progressive encephalopathy, weakness, and fevers diagnosed with West Nile virus-meningoencephalitis. His hospital course was complicated by hypercapnic respiratory failure and septic shock leading to oligo-anuric ATN initiated on continuous veno-venous hemodialysis for acidosis and volume overload. His Cr trend:

As the patient’s mental status and respiratory status started to improve, his wife asked: “Will he need dialysis for the rest of his life?”

Case 4 -- AKI-D Significance

- 6-7% of ICU patients
- Independently associated with short-term mortality
- Associated with long-term complications:
  - CKD, ESRD
  - CVD: HTN, CHF, CHD
  - Stroke

Cerda Lancet 2015; Lo KI 2009; Odutayo JASN 2017; Walker JASN 2006

Case 4 – AKI-D Recovery Probabilities

<table>
<thead>
<tr>
<th>Pre-admission eGFR (mL/min/1.73m²)</th>
<th>Renal Recovery (among survivors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>100% (Schiffl NDT 2006)</td>
</tr>
<tr>
<td>24-5</td>
<td>84% (Lo KI 2009)</td>
</tr>
<tr>
<td>15-29</td>
<td>58% (Hsu CJASN 2009)</td>
</tr>
<tr>
<td>15-29</td>
<td>37% (Hsu CJASN 2009)</td>
</tr>
</tbody>
</table>
42 y/o male with PMH of HTN and obesity admitted for progressive encephalopathy, weakness, and fevers diagnosed with West Nile virus-meningoencephalitis \(\rightarrow\) AKI-D. I told the patient’s wife that he has ~80% chance coming off dialysis by 3-6 months after discharged from the hospital.
Case 5 – A Case of Covid-19

• 50 y/o female with PMH of HTN, DM, CKD 4 with nephrotic range proteinuria (last creatinine check 2020 was 2.3) admitted for mechanical fall due to weakness and found to have febrile illness with Covid (+ vaccinated with Janssen). No NSAID or other nephro-toxin exposure. We are consulted for elevated creatinine:

8/2020 7/2021

Case 5 – A Case of Covid-19


Case 5 – A Case of Covid-19

• Maybe this is collapsing FSGS:
Summary

1) Be on the lookout for non-ATN AKI
2) Don’t be afraid to give loop diuretic with creatinine trending up to manage ATN
3) Absolute level of BUN ≠ yes/no uremia
4) Oliguria, ingestion, and uremia are the real indications for RRT
5) For AKI-D, ~80% for GFR >=45, ~40% for GFR <45 will come off dialysis 3-6 months after discharge
6) Covid-19 likely has some direct kidney injury effect

References

STARRT-AKI Investigators; Canadian Critical Care Trials Group; Australian and New Zealand Intensive Care Society; Clinical Trials Network of the United Kingdom; Canadian Critical Care Trials Group; Canadian Network for Clinical Trials in Crohn’s Disease Trial Network; Clinical Trials Network of the United Kingdom; Elsevier; Verlag; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; Elsevier; El...
Updates in Perioperative Medicine

- Perioperative anticoagulation – increasing clarity
- Preoperative echo – useful or overused?
- Postoperative atrial fibrillation – anticoagulation?
- Surgery after COVID-19 – because of course
- Curbside consultation – risks for patient and provider

Managing Perioperative Anticoagulation

A head & neck surgeon asks how to manage anticoagulation in two patients on warfarin who will have major surgery next week.

- One patient has atrial fibrillation due to HTN
- The other has a mechanical aortic valve prosthesis
- Neither has any other relevant comorbidity

“Should we bridge with LMWH while their warfarin is held?”

1. Bridge for AVR only
2. Bridge for AF only
3. Bridge for both
4. Bridge for neither

BRIDGE Trial

Randomized trial of perioperative bridging for AF

- 1884 patients taking warfarin for atrial fibrillation or flutter
- Excluded: mechanical valve, stroke < 12 wks, cardiac & neurologic surgery
- Randomized to bridging with LMWH or placebo when warfarin interrupted for major or minor procedures
- Outcomes: 30-day arterial thromboembolism & bleeding

Douketis JD et al. NEJM, 2015; 373:823-33
BRIDGE Trial

<table>
<thead>
<tr>
<th></th>
<th>Bridged</th>
<th>No Bridge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embolic Event</td>
<td>0.3%</td>
<td>0.4%</td>
</tr>
<tr>
<td></td>
<td>Non-inferior</td>
<td></td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>3.2%</td>
<td>1.3%</td>
</tr>
<tr>
<td></td>
<td>NNH = 53</td>
<td></td>
</tr>
<tr>
<td>Minor Bleeding</td>
<td>21%</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td>NNH = 12</td>
<td></td>
</tr>
</tbody>
</table>

Douketis JD et al. NEJM, 2015; 373:823-33

PERIOP 2 Trial

Randomized trial of bridging for AF or mechanical valve
- 1471 patients taking warfarin for atrial fib/flutter, mechanical valve, or both undergoing major or minor procedure
- Excluded mechanical valve patients with: prior stroke/TIA, multiple valves, or Starr-Edwards valve
- All patients received dalteparin prior to surgery
- Randomized to dalteparin or placebo after surgery
  - Therapeutic dose given after low-bleeding risk procedures
  - Prophylactic dose given after high-bleeding risk procedures
- Outcomes: 90-day thromboembolism & bleeding rates

Kovacs MJ et al. BMJ 2021;373:n1205

PERIOP 2 Trial

<table>
<thead>
<tr>
<th>90-day Outcome</th>
<th>Bridge</th>
<th>No Bridge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major thromboembolism</td>
<td>1.0%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.3%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

- No significant difference in TE & bleeding risk in all comparisons
- Outcomes similar for patients with AF and mechanical valves
- Only 1 out of the 304 patients with mechanical valve had a TIA

Kovacs MJ et al. BMJ 2021;373:n1205

Conclusions from BRIDGE & PERIOP 2

Bridging does not reduce risk of thromboembolism:
- Strong evidence for atrial fibrillation
- Fair evidence for mechanical valves
- Baseline TE risk is low without bridging

Bridging likely increases the bleeding risk:
- Small effect on major bleeds, larger effect on minor bleeds

Caveat:
- Studies had relatively few patients with very high TE risk or bleeding risk
**ACC Guideline for AF (2017)**

<table>
<thead>
<tr>
<th>Bleeding Risk*</th>
<th>Normal Thrombotic Risk</th>
<th>Elevated Thrombotic Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Thrombotic Risk</td>
<td>Bridge</td>
<td>Clinical Judgment</td>
</tr>
<tr>
<td>CHA2DS2-VASc = 7+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mod Thrombotic Risk</td>
<td>Clinical Judgment</td>
<td>No Bridge</td>
</tr>
<tr>
<td>CHA2DS2-VASc = 5-6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Thrombotic Risk</td>
<td>No Bridge</td>
<td></td>
</tr>
<tr>
<td>CHA2DS2-VASc = 1-4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Bleeding risk elevated if major bleed or ICH < 3 months, platelets low or abnormal, aspirin use, supratherapeutic INR, or prior bleeding with bridging or similar surgery.

---

**How to PAUSE a DOAC**

**Perioperative Anticoagulation Use for Surgery Evaluation**
- International study of 3007 elective surgery patients taking apixaban, rivaroxaban or dabigatran for atrial fibrillation
- Interrupted & resumed DOAC using standardized protocol
- Considers surgical bleeding risk and (for dabigatran) CrCl
- No bridging was permitted

**PAUSE Trial Results**

- Average CHADS2 = 2.1 (CHA2DS2-VASc = 3.4)
- Patients having high bleeding risk surgery = 33%

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Bleeding</td>
<td>0.9%</td>
<td>1.35%</td>
<td>1.85%</td>
</tr>
<tr>
<td>Arterial Thromboembolism</td>
<td>0.6%</td>
<td>0.16%</td>
<td>0.37%</td>
</tr>
</tbody>
</table>

**Dabigatran (CrCl > 50), Apixaban, Rivaroxaban:**

<table>
<thead>
<tr>
<th></th>
<th>Day -3</th>
<th>Day -2</th>
<th>Day -1</th>
<th>OR Day +1</th>
<th>Day +2</th>
<th>Day +3</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Bleed Risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Low Bleed Risk</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Dabigatran with CrCl < 50**

<table>
<thead>
<tr>
<th></th>
<th>Day -5</th>
<th>Day -4</th>
<th>Day -3</th>
<th>Day -2</th>
<th>Day -1</th>
<th>OR Day +1</th>
<th>Day +2</th>
<th>Day +3</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Bleed Risk</td>
<td></td>
<td></td>
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<tr>
<td>Low Bleed Risk</td>
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</tbody>
</table>

Preoperative Echocardiography

You perform an urgent preoperative evaluation on an 83-y.o. woman with a hip fracture. She has history of mild dementia, remote stroke, diabetes, and hypertension. She reports no dyspnea or angina. Functional capacity unknown, as she is sedentary. Cardiopulmonary exam is normal.

You wonder whether to obtain a transthoracic echo.

1. No, it’s not indicated
2. Yes, it is indicated
3. Yes, because Anesthesia will insist

Guideline Indications for Preop Echo

- Suspect moderate or greater valvular stenosis or regurgitation if no echo in past year or significant clinical change since then (Recommended)
- Heart failure with worsening dyspnea or other change in clinical status (Reasonable)
- Dyspnea of unknown origin (Reasonable)
- Reassessment of LV function in clinically stable patients with previous documented LV dysfunction may be considered if there has been no assessment within 1 year (Not unreasonable)

ACC/AHA Guideline Circulation. 2014;130:2215–2245

Preoperative TTE for Urgent Surgery

Japanese national database of 66,620 hip fracture surgery patients:

- 52% underwent preoperative TTE
- Patient having preop TTE were older & sicker
- Patients were matched using propensity score

<table>
<thead>
<tr>
<th></th>
<th>TTE</th>
<th>No TTE</th>
<th>All N.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital Mortality</td>
<td>1.65%</td>
<td>1.74%</td>
<td></td>
</tr>
<tr>
<td>Cardiac Complications</td>
<td>0.39%</td>
<td>0.40%</td>
<td></td>
</tr>
<tr>
<td>ICU Admission</td>
<td>0.46%</td>
<td>0.37%</td>
<td></td>
</tr>
</tbody>
</table>


Postoperative Atrial Fibrillation

You evaluate a 70-y.o. woman with h/o HTN who develops new postoperative (POAF) atrial fibrillation after total knee arthroplasty. You slow her rate with metoprolol, and she converts back into NSR overnight. Echocardiogram shows normal LV function, normal valves, and mild LAE. Her CHA2DS2VASc = 3.

Would you recommend long-term anticoagulation?

1. No
2. Yes
3. Let the PCP decide
**POAF Predicts Further AF & Stroke**

- Observational study of 452 patients with new POAF
- Matched by age, sex, year of surgery, and type of surgery with patient without POAF
- Followed out for 5 years after surgery

<table>
<thead>
<tr>
<th>5-year Event Rate</th>
<th>POAF</th>
<th>No POAF</th>
<th>Adj. HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subsequent AF diagnosis</td>
<td>51%</td>
<td>12%</td>
<td>7.9 [4.8-13]</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>10.7%</td>
<td>6.0%</td>
<td>2.7 [1.4-5.3]</td>
</tr>
<tr>
<td>All Cause Mortality</td>
<td>46.6%</td>
<td>37.2%</td>
<td>1.7 [1.3-2.1]</td>
</tr>
</tbody>
</table>

Siontis KC et al. JAMA. 2020;324(9):871-878

**POAF: Does Anticoagulation Help?**

- Retrospective study identified 22,007 patients with new POAF
- Looked at rates of stroke and bleeding based on whether they were prescribed anticoagulation
- Stratified based on CHA2DS2-VASc & HAS-BLED

**Stroke Risk Conclusions**

Long-term stroke risk from POAF underappreciated:
- Patients with POAF have 2-fold (adjusted) risk of stroke compared to surgical patients who do not develop AF
- Stroke risk for POAF may be similar to patients with usual, non-surgical NVAF
- Benefits of anticoagulation are unproven

What to do?
- Guidelines recommend treating POAF as regular AF
- Evidence lacking for options: AC? Rhythm monitoring?
You discharge a 50-y.o. obese woman after a 5-day admission for COVID-19 pneumonia. She is now oxygenating well, but still very tired and a little short of breath. On the way out, she says: “I'm scheduled for a gastric bypass in 4 weeks. Can I still have surgery?”

1. Yes, that should be okay
2. Only if your symptoms resolve
3. No...really just don’t

Prospective cohort study of surgical cases in Oct 2020:
- 3127 patients (2.2%) had prior COVID-19 infection
- Adjusted mortality for non-infected patients = 1.5%

Weeks between COVID-19 infection and Surgery

- 0 to 2
- 4 to 6
- > 7

No COVID

Adjusted Mortality (O.R.)

Higher mortality when surgery performed < 7 weeks after COVID-19 infection:
- Regardless of age, health, urgency/intensity of surgery
- Even if asymptomatic infection (though not as high)
- Even after 7 weeks, mortality higher in patients with ongoing or resolved symptoms compared with asymptomatic cases
- Same pattern observed for postop pulmonary complications

Surgical planning should consider: severity of infection; ongoing symptoms; comorbid & functional status, before and after SARS-CoV-2 infection; clinical priority and risk of disease progression; and complexity of surgery
- Avoid elective surgery within 10 days of mild/mod infection & 15-20 days of severe infection
- Elective surgery should not be scheduled within 7 weeks of diagnosis, unless outweighed by the risk of delaying
- Delaying surgery beyond 7 weeks should be considered in patients with persistent symptoms

COVIDSurg Collaborative. Anaesthesia 2021, 76, 748–758

El-Boghdadly K et al. Anaesthesia 2021, 76, 940–946
Are Curbside Consults Safe?

A surgeon calls you to discuss admission for a patient with a suspected infection. Based on this conversation, it doesn’t sound like admission is necessary. However, you wonder whether you’re liable if you give bad advice on a patient you’re not treating.

1. You’re safe; there’s no duty to treat
2. Put your lawyer on speed-dial
3. What state am I practicing in?

Curbside Consults

Studied 47 requests for curbside advice to hospitalist
- Curbside consultant could ask questions ad lib
- Made recommendations without seeing patient or chart
- Different hospitalist performed formal, in-person evaluation

Questions:
- Did curbside consultant obtain accurate information?
- Did advice and management differ?

Curbside vs. Formal Medicine Consult

Compared to formal consultation, how often did curbside evaluation lead to:

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete clinical information</td>
<td>34%</td>
</tr>
<tr>
<td>Inaccurate clinical information</td>
<td>28%</td>
</tr>
<tr>
<td>Any difference in management</td>
<td>60%</td>
</tr>
<tr>
<td>Major difference in management</td>
<td>36%</td>
</tr>
</tbody>
</table>

Liability from Curbside Consults

Traditional view:
- Physician-patient relationship ("duty to care") required for malpractice liability
- Purely curbside consultation does not establish treatment relationship – but deeper involvement (chart review, visiting patient, documentation, care coordination) blurs the line

Minnesota & "reasonably foreseeable":
- "duty arises…when the physician provides medical advice and it is foreseeable that the third party will rely on [it]"
Curbside with Caution

Be wary when giving (or requesting) informal advice:
• Only for basic, generic questions
• Avoid in unstable or critically ill patients
• If you’re asking a lot of questions, do a formal consult
• Offer to perform formal consultation; insist on it if “curbsided” again on same patient
• Don’t visit patient, write orders, review chart, or submit bill

Take Home Points

1. Most patients on anticoagulation of atrial fibrillation or mechanical valves don’t require perioperative bridging
2. Echocardiography has a role in preoperative evaluation, but it's smaller than you might think
3. Postoperative atrial fibrillation predicts future stroke and mortality; benefit vs. risks of anticoagulation uncertain
4. Delay elective surgery at least 7 weeks after COVID-19 diagnosis if possible, even longer if still symptomatic
5. Exercise caution when providing curbside advice

Thank You

Quinny.Cheng@ucsf.edu
Disclosures

- No Conflicts of Interest
- No Financial Disclosures
- Krishan.soni@ucsf.edu

Outline

- Coronary Artery Disease
  - Aspirin and prevention of coronary artery disease (CAD)
  - Antiplatelet therapy for secondary prevention
  - Management of combined anticoagulation and antiplatelet agents

- Heart Failure
  - Updates in Medical Therapies: ARNI and SGLT2 Inhibitors
  - Treatment of Functional Mitral Regurgitation
  - Putting it all together: Rethinking the algorithm for HFrEF

Cardiology Pearls for the Hospitalist

- Major Society Guideline Updates 2016-2021
- Clinical Trials Published 2016-2021

Address common questions from Internal Medicine / Hospitalist Community
Acronyms

- ACS: Acute Coronary Syndrome
- BMS: Bare Metal Stent
- CAD: Coronary Artery Disease
- CABG: Coronary Artery Bypass Graft Surgery
- DAPT: Dual Antiplatelet Therapy
- DES: Drug Eluting Stent
- DOAC: Direct Oral Anticoagulant
- HF: Heart Failure
- MR: Mitral Regurgitation
- PCI: Percutaneous Coronary Intervention
- SIHD: Stable Ischemic Heart Disease
- VKA: Vitamin K Antagonist

Outline

- **Coronary Artery Disease**
  - Aspirin and prevention of coronary artery disease (CAD)
  - Antiplatelet therapy for secondary prevention
  - Management of combined anticoagulation and antiplatelet agents

- **Heart Failure**
  - Updates in Medical Therapies: ARNI and SGLT2 Inhibitors
  - Transcatheter Repair for Mitral Regurgitation
  - Putting it all together: Rethinking the algorithm for HF
def. EF
Dr. -  
I just saw on the TV news tonight that for people over 65 years old that the daily dose of baby aspirin is not necessary and may even be counter productive. They are effective for people in their 40’s.  
Should I continue to take my daily dose of baby aspirin?  
Please advise. Thank you

Hi Dr. -  
I wanted to see if you think it would be reasonable to discontinue Mr. XX aspirin. His MI was remote in 1994 and he continues on rivaroxaban for afib. Would love to hear your thoughts.  
Anticoagulation Pharmacist

---

**USPSTF 2016 Guidance**

**Recommendation Summary**

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults aged 50 to 69 years without a 10% or greater 10-year cardiovascular disease (CVD) risk</td>
<td>The USPSTF recommends discontinuing low-dose aspirin use for the primary prevention of CVD and colorectal cancer (CRC) in adults aged 50 to 69 years who have a 10% or greater 10-year CVD risk</td>
<td>B</td>
</tr>
<tr>
<td>Adults aged 70 years or greater</td>
<td>The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or greater should be an individual one</td>
<td>C</td>
</tr>
<tr>
<td>Adults younger than 50 years</td>
<td>The current evidence is limited to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years</td>
<td>I</td>
</tr>
<tr>
<td>Adults aged 70 years or older</td>
<td>The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or older</td>
<td>I</td>
</tr>
</tbody>
</table>

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**USPSTF 2021 DRAFT Guidance**

**Recommendation Summary**

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<tr>
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<td>The decision is to discontinue low-dose aspirin use for the primary prevention of CVD in adults aged 50 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one</td>
<td>C</td>
</tr>
<tr>
<td>Adults age 80 years or older</td>
<td>The USPSTF recommends against initiating low-dose aspirin use for the primary prevention of CVD in adults age 80 years or older</td>
<td>D</td>
</tr>
</tbody>
</table>

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**Primary Prevention: Aspirin**

**ARRIVE Trial**

**Clinical Question:**

What is the clinical benefit of 100 mg per day of aspirin in reducing the risk of cardiovascular death, myocardial infarction, unstable angina, stroke, or transient ischemic attack in patients at moderate risk of cardiovascular events without diabetes?

**Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial**

Primary Prevention: Aspirin
ARRIVE Trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aspirin</th>
<th>Placebo</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Outcome of Cardiovascular Death, Myocardial Infarction, Unstable Angina, Stroke, or TIA</td>
<td>4.3%</td>
<td>4.5%</td>
<td>p = 0.60</td>
</tr>
<tr>
<td>Gastrintestinal Bleeding</td>
<td>0.97%</td>
<td>0.43%</td>
<td>p = 0.0007</td>
</tr>
</tbody>
</table>

Primary Prevention: Aspirin
ASCEND Trial

Clinical Question:
What is the clinical benefit of 100 mg per day of aspirin in reducing the risk of vascular death, myocardial infarction, or stroke/transient ischemic attack in patients with known diabetes but no history of cardiovascular disease?


Primary Prevention: Aspirin
ASCEND Trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aspirin</th>
<th>Placebo</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Outcome of Cardiovascular Death, Myocardial Infarction, Stroke, or TIA</td>
<td>8.5%</td>
<td>9.6%</td>
<td>p = 0.01</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>4.1%</td>
<td>3.2%</td>
<td>p = 0.003</td>
</tr>
</tbody>
</table>

Aspirin resulted in a 1.1% absolute risk reduction in major adverse cardiovascular events.

Aspirin resulted in a 0.9% absolute increase in major bleeding.

NNT: 91
NNH: 111
Primary Prevention: Aspirin
ASCEND Trial

What about cancer?...

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Placebo</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Cancer</td>
<td>2.0%</td>
<td>2.0%</td>
<td>p = 1</td>
</tr>
<tr>
<td>All Cancer</td>
<td>11.6%</td>
<td>11.5%</td>
<td>p = 0.98</td>
</tr>
</tbody>
</table>

No Benefit in Reducing Fatal or Non-Fatal Cancer

Primary Prevention: Aspirin

Aspirin and All Cause Mortality in 14 Primary Preventions Trials

An aspirin a day...

Should not routinely be prescribed to patients without prior cardiovascular events due to a lack of clinical benefit and/or increased risk of bleeding that offsets the reduction in cardiovascular events
Primary Prevention: Aspirin  
2019 AHA/ACC Guidelines

<table>
<thead>
<tr>
<th>4.6. Aspirin Use</th>
<th>Recommendations for Aspirin Use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary Artery Disease</strong></td>
<td><strong>Aspirin and prevention of coronary artery disease (CAD)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Antiplatelet therapy for secondary prevention</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Management of combined anticoagulation and antiplatelet agents</strong></td>
</tr>
<tr>
<td><strong>Heart Failure</strong></td>
<td><strong>Updates in Medical Therapies: ARNI and SGLT2 Inhibitors</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Transcatheter Repair for Mitral Regurgitation</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Putting it all together: Rethinking the algorithm for HFrEF</strong></td>
</tr>
</tbody>
</table>

Antiplatelet therapy in patients with known Coronary Artery Disease (CAD)

**ACC/AHA GUIDELINES UPDATE**

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

<table>
<thead>
<tr>
<th>Oral Antiplatelet Agents</th>
<th>Aspirin</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>Ticagrelor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>ACS Post PCI</td>
<td>Stroke</td>
<td>ACS Post PCI</td>
<td>Stroke</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>325 mg</td>
<td>DAILY</td>
<td>300-600 mg</td>
<td>DAILY</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td>NSAAID</td>
<td>2nd gen Thienopyridine</td>
<td>2nd gen Thienopyridine</td>
<td>CTPT</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>IRREVERSIBLE COX 1</td>
<td>IRREVERSIBLE P2Y12</td>
<td>IRREVERSIBLE P2Y12</td>
<td>REVERSIBLE P2Y12</td>
</tr>
<tr>
<td><strong>Peak Effect</strong></td>
<td>1-3 hours</td>
<td>6 hours</td>
<td>4 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td><strong>CYP Metabolism</strong></td>
<td>NA</td>
<td>2C19</td>
<td>3A4</td>
<td>3A4/5</td>
</tr>
<tr>
<td><strong>FDA Approval</strong></td>
<td>1997</td>
<td>2009</td>
<td>2011</td>
<td><strong>Generic Approval</strong></td>
</tr>
</tbody>
</table>
Aspirin dosing in patients with Coronary Artery Disease

Higher doses of aspirin are associated with bleeding and no increased anti-ischemic benefit.
When used with ticagrelor, aspirin doses of >100 mg are contraindicated.

Duration of dual antiplatelet therapy (DAPT)

- Duration of DAPT depends on:
  - Underlying condition
  - Treatment provided

Duration of dual antiplatelet therapy (DAPT) in patients with ACS

ACS = 1 year
Stopping early at 6 months

Duration of dual antiplatelet therapy (DAPT) in patients with SIHD

PCI with Bare Metal Stent (BMS) 1 MONTH
Stopping early at 3 months
PCI with Drug Eluting Stent (DES) 6 MONTHS
Duration of Antiplatelet Therapy
TWILIGHT Trial

Clinical Question:
Can aspirin be safely discontinued from the dual antiplatelet regimen after three months in patients undergoing PCI?

Regimen:
Aspirin 81 + Ticagrelor x 12 months
OR
Aspirin 81 + ticagrelor x 3 months then ticagrelor + placebo x 9 months

ASA + Ticagrelor
 ASA (3 mos) Ticagrelor (12 mos)

<table>
<thead>
<tr>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>7.1%</td>
</tr>
<tr>
<td>Composite</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

Bleeding Composite

Antiplatelet Therapy Summary
- When used, dose of Aspirin for all patients with CAD is 81 mg daily
- Duration of DAPT:
  - ACS Patients: 1 YEAR for ALL (with/without stent)
  - SIHD (Stable Ischemic Heart Disease) Patients:
    - Drug Eluting Stent (DES): 6 MONTHS
    - Bare Metal Stent (BMS): 1 MONTH
- Stopping Early:
  - New trials show that shorter durations of aspirin therapy after stenting may be effective and result in lower bleeding risk

Outline
- Coronary Artery Disease
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  - Putting it all together: Rethinking the algorithm for HF with EF
Management of combined anticoagulant and antiplatelet therapy

Long-term treatment with oral anticoagulants is necessary in patients with:
- Mechanical heart valves
- Many with atrial fibrillation

20–30% of these patients have concomitant ischemic heart disease that requires PCI with stenting and subsequent antiplatelet therapy.

The combination of oral anticoagulants and antiplatelets is associated with a high annual risk (4–16%) of fatal and non-fatal bleeding episodes.

What is the indication for triple therapy?
- Recent ACS (<1 year)
- Recent PCI (< 6 months)
- Chronic Ischemic heart disease
- Stroke
- Peripheral vascular disease

Need to balance risk of thrombotic / ischemic events with bleeding
Use risk scores to help assess:
- CHADS2-VASC for stroke risk in AF
- HAS-BLED for bleeding risk

Multiple medical options for therapy
- Aspirin
- P2Y12 Inhibitors
- Clopidogrel
- Ticagrelor
- Prasugrel

- Coumadin
- Dabigatran
- Rivaroxaban
- Apixaban
- Edoxaban

What is the safety and efficacy of each medication?
What combinations offer the greatest reduction in ischemic / thrombotic events?
Which combinations have the lowest bleeding risk?

Four recent trials:
- WOEST (2013)
- PIONEER AF (2016)
- RE DUAL PCI (2017)
- AUGUSTUS (2019)
Triple therapy associated with higher bleeding without thrombotic protection

**WOEST**
- Coumadin + Clopidogrel: 19% + Clopidogrel + Aspirin: 11%
- Coumadin + Clopidogrel + Aspirin: 11%

**PIONEER AF PCI**
- Rivaroxaban 15 mg Daily + P2Y12: 17% + Aspirin: 6.5%
- Rivaroxaban 2.5 mg BID + P2Y12 + Aspirin: 18% 5.6%
- Coumadin + P2Y12 + Aspirin: 27% 6%

**RE DUAL PCI**
- Dabigatran 110 mg BID + P2Y12: 15% + Aspirin: 13%
- Dabigatran 150 mg BID + P2Y12: 20% 13%
- Coumadin + P2Y12 + Aspirin: 28% 14%

**Preferred options in United States**


**Clinical Question:**
What is the safest and most effective medical regimen for patients with atrial fibrillation and chronic coronary artery disease (angiography with no intervention or PCI/CABG > 1 year prior)?

**Rivaroxaban + Placebo**
- Composite Outcome of Stroke, Embolism, Myocardial Infarction, Unstable Angina requiring revasc, or Death: 4.14% vs 5.75%; p = <0.001
- Major Bleeding: 1.62% vs 2.76%; p = 0.01

**Long Term Anticoag and Antiplatelet**
**AFIRE Trial**

- Patients with atrial fibrillation and stable coronary artery disease more than 1 year after revascularization or in those with angiographically confirmed coronary artery disease not requiring revascularization
- Rivaroxaban monotherapy was noninferior to combination with respect to cardiovascular events and death from any cause
- Rivaroxaban monotherapy was superior with respect to major bleeding.
All this evidence now incorporated into the 2020 ACC Expert Consensus Pathway

**Bottom Line** regarding antithrombotic therapy

- **Anticoagulant**
  - DOAC strongly preferred over Coumadin if the patient is a candidate
  - DOACs should not be used for patients with:
    - Mechanical heart valves
    - Atrial fibrillation and mitral stenosis

- **P₂Y₁₂**
  - Clopidogrel preferred over other P₂Y₁₂ agents

- **Aspirin**
  - Little need for triple therapy, can usually drop aspirin in favor of DOAC + P₂Y₁₂ alone

- **Long Term**
  - Drop BOTH antiplatelet agents (oral anticoagulation alone)

**The Role for Aspirin in 2021**

<table>
<thead>
<tr>
<th>Primary Prevention</th>
<th>Recent PCI / Acute Coronary Syndrome</th>
<th>Chronic Coronary Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not on Anticoagulation</td>
<td>No Antiplatelet</td>
<td>Dual Antiplatelet (P₂Y₁₂ + Aspirin) 3-12 months</td>
</tr>
<tr>
<td>Concurrent Anticoagulation</td>
<td>AC Alone (DOAC)</td>
<td>DOAC + Single Antiplatelet (P₂Y₁₂) 6-12 months</td>
</tr>
</tbody>
</table>
Doc, Should I still take my aspirin?

<table>
<thead>
<tr>
<th></th>
<th>Aspirin?</th>
<th>Therapy in 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Prevention</strong></td>
<td>Not Routinely</td>
<td>Lifestyle</td>
</tr>
<tr>
<td><strong>After Acute Coronary Syndrome (ACS)</strong></td>
<td>As short as 3 months</td>
<td>$P_{2Y12}$ for 1 Year</td>
</tr>
<tr>
<td>- Recent MI / PCI &lt; 1 year</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ACS + Atrial fibrillation</strong></td>
<td>NO</td>
<td>DOAC indefinitely</td>
</tr>
<tr>
<td><strong>Chronic Coronary Disease</strong></td>
<td>YES</td>
<td>Aspirin Alone</td>
</tr>
<tr>
<td>- MI &gt;1 year / PCI &gt;6 mos</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic Coronary Disease and Atrial Fibrillation</strong></td>
<td>NO</td>
<td>DOAC Alone</td>
</tr>
</tbody>
</table>

Outline

- **Coronary Artery Disease**
  - Aspirin and prevention of coronary artery disease (CAD)
  - Antiplatelet therapy for secondary prevention
  - Management of combined anticoagulation and antiplatelet agents

- **Heart Failure**
  - Updates in Medical Therapies: ARNI and SGLT2 Inhibitors
  - Transcatheter Repair for Mitral Regurgitation
  - Putting it all together: Rethinking the algorithm for HFmr EF

Management of Heart Failure in 2021

- **Medications**
  - Diuretics
  - Digoxin
  - ACE inhibitors, beta blockers

- **Surgery**
  - Coronary-artery bypass grafting
  - Heart valve repair or replacement
  - Heart transplant

- **Lifestyle**
  - Comply with heart healthy diet
  - Comply with exercise

Standard of Care and State of the Art in 2021

- **Medical Therapy**
  - Beta Blockers
  - ACE Inhibitors/ARBs
  - Mineralocorticoid Receptor Antagonists
  - Angiotensin Receptor / Neprilysin Inhibitor (ARNI)
  - Sodium Glucose co-transporter 2 Inhibitors (SGLT2i)

- **Intracardiac Devices**
  - Implantable Cardiac Defibrillators
  - Cardiac Resynchronization Therapy
  - Pulmonary Artery Pressure sensors

- **Management of Valve Disease** (particularly functional mitral regurgitation)
  - Surgical Therapies
  - Percutaneous Interventional Therapies
ARNI Mechanism
Angiotensin Receptor / Neprilysin Inhibitor (ARNI) = Sucabitril/Valsartan

ARNI in heart failure with reduced EF

- Clinical Question: Does sucabitril/valsartan improve the risks of death or rehospitalization compared to enalapril in patients with heart failure?

ARNI in heart failure with reduced EF
Patients on ARNI had significantly reduced rates of death and hospitalization for heart failure.

Double Blind, Randomized
- 8442 Patients
- Class II, III, IV HF
- EF <= 40%
- All on baseline therapy

Primary Outcome: composite of death or hospitalization for HF.
Stopped early at 27 months
ARNI group had more angioedema and hypotension.

ARNI added to HF guidelines in 2016

Recommendations for Renal-Angiotensin System Inhibition With ACE Inhibitor orARB or ARNI

**Cor**

<table>
<thead>
<tr>
<th>Recommendations</th>
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</thead>
<tbody>
<tr>
<td><strong>ACE</strong> A+B</td>
</tr>
<tr>
<td><strong>ARB</strong> A+B</td>
</tr>
</tbody>
</table>

- The clinical strategy of inhibition of the renin-angiotensin system with ACE inhibitors (ACE; A) or ARBs (ARB; B) is based on evidence of benefit of ACE inhibitors (ACE; A) or ARBs (ARB; B) in patients with chronic HF.
- ACE inhibitors (ACE; A) or ARBs (ARB; B) are recommended for patients with chronic HF, as they reduce mortality and morbidity.
- **ACE** inhibitors (ACE; A) or ARBs (ARB; B) are recommended for patients with chronic HF, as they reduce mortality and morbidity.

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13 | [footer text here]
Current recommendation for ARNI use

Indications for Use of an ARNI

- HF/EF (EF ≤ 40%)
- NYHA class III-IV HF
- Administered in conjunction with a background of GDMT for HF in place of an ACEI or ARB

<table>
<thead>
<tr>
<th>ARNI</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacubitril/valsartan</td>
<td>24/26 mg-48/51 mg twice daily</td>
<td>97/103 mg twice daily</td>
</tr>
</tbody>
</table>

SGLT2 Mechanism
Sodium Glucose Co-Transporter 2 Inhibitor

Clinical findings:
- Plasma glucose
- Body weight
- Blood pressure
- Plasma uric acid
- Glomerular hyperfiltration

SGLT2 Pleotropic Effects
**Clinical Question**: Does empagliflozin (SGLT2i) improve the risks of death or rehospitalization compared in patients with heart failure with reduced EF?

**Findings**
- Patients on Empagliflozin had significantly reduced rates of death and hospitalization for heart failure.
- Patients had a lower rate of decline in GFR.

**Study Details**
- **Double Blind, Randomized**
- **3730 Patients**
- **Class II, III, IV HF**
- **EF <= 40%**
- **All on baseline therapy**

**Primary Outcome**: composite of death or hospitalization for HF.

Findings occurred in patients with and without diabetes.
**Outline**

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  - Treatment of Functional Mitral Regurgitation
  - Putting it all together: Rethinking the algorithm for HFr
d

**Current recommendation for SGLT2i**

**Indications for Use of an SGLT2 Inhibitor**
- HFpEF (EF <=40%) with or without diabetes
- NYHA Class III-IV HF
- Administered in conjunction with a background of GDMT for HF

<table>
<thead>
<tr>
<th>SGLT2 inhibitors</th>
<th>Starting Dose</th>
<th>Target Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>10 mg daily</td>
<td>10 mg daily</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>10 mg daily</td>
<td>10 mg daily</td>
</tr>
</tbody>
</table>

**Functional mitral regurgitation**

Dilation of a failing left ventricle can result in significant mitral regurgitation (MR).

MR increases left atrial pressures and can result in heart failure symptoms.

If MR does not resolve with medical management of HF, additional therapies may be warranted.
Clinical Question: Do patients who have heart failure with reduced EF and symptomatic moderate to severe mitral regurgitation benefit from transcatheter mitral valve repair in addition to guideline directed medical therapy?

Randomized controlled trial
- 614 patients
- 78 sites US and Canada
- HF symptomatic mod-sev MR
- All on maximum therapy

Primary Efficacy Outcome: Hospitalization for HF within 24 mos
Primary Safety Outcome: Freedom from complications at 12 mos

Patients who underwent mitral repair had a significant decline in hospitalization for heart failure.

Patients who underwent mitral repair had a significant decline in death with low procedural complication rate.
Outline

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  - Putting it all together: Rethinking the algorithm for HFrEF
Steps in managing HF with reduced EF

(1) Start ACEi/ARB/ARNI (ARNI preferred)
(2) Start guideline directed beta blocker
(3) Use diuretic as needed for volume overload
(4) Up titrate (1) and (2) as tolerated every 2 weeks with monitoring
(5) Start aldosterone antagonist if eGFR > 30 ml/min/1.73m and K < 5.0 meq/dL
(6) Start SGLT2 inhibitor if eGFR >20 ml/min/1.73m
(7) Repeat transthoracic echocardiogram in 2-3 months
(8) Refer for ICD/CRT therapies if EF remains low and patient qualifies
(9) Refer to valve center for consideration of valve therapy if significant mitral regurgitation

Outline

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Take Home Points

- Coronary Artery Disease
  - Aspirin should not routinely be prescribed to patients without prior cardiovascular events
  - When used for treating CAD, dose of Aspirin is 81 mg daily
  - Duration of DAPT:
    - ACS Patients: 1 YEAR for ALL (with/without stent)
    - SIHD (Stable Ischemic Heart Disease) Patients:
      - Drug Eluting Stent (DES): 6 MONTHS
      - Bare Metal Stent (BMS): 1 MONTH
  - For patients requiring anticoagulation and antiplatelet therapies
    - Ensure there is an indication for both
    - DOACs are preferred over coumadin
    - Clopidogrel preferred over other P2Y12 agents
    - Aspirin can usually be omitted from the regimen

- Heart Failure
  - For your patients with heart failure and reduced EF:
    - ARNI confer a benefit for mortality and reduced hospitalizations
    - SGLT2 Inhibitors benefit patients with and without DM
    - Severe functional mitral regurgitation that has not responded to optimal medical therapy can be treated with transcatheter valve repair to reduce death and heart failure rehospitalization
Questions?
Covid-19 and the Transformation of Healthcare

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Disclosures

- Dr. Wachter serves on the board of directors of The Doctors Company (malpractice insurer) and on the scientific advisory boards of Teladoc (telemedicine provider), Amino (help employers choose healthcare providers), Curai (AI-enabled urgent care), EarlySense (bed-covering that measures vital signs), Commure (interoperability platform), and Notable (digital process automation). He also advises the San Francisco 49ers football team and SCOR (life insurance company) on Covid-19. He holds the Benioff Chair in Hospital Medicine from Marc and Lynne Benioff.

Before we start, let’s check in to be sure everybody is feeling OK...

Talk Roadmap

- A few thoughts on the current state of the pandemic and the problems it has exposed in our politics and society
- A few tech innovations that were accelerated by Covid
  - Telemedicine, dashboards
  - Plus a few that might have hit the tipping point, but didn’t
- Entering the post-EHR era: why and what that means
- The future of healthcare’s digital transformation
America’s Unique Response

“Aspects of America’s identity may need rethinking after COVID-19. Many of the country’s values have seemed to work against it during the pandemic. Its individualism, exceptionalism, and tendency to equate doing whatever you want with an act of resistance meant that when it came time to save lives and stay indoors (and wearing masks & getting vaccinated), some people flocked to bars and clubs (and didn’t & didn’t). Having internalized years of anti-terrorism messaging following 9/11, Americans resolved to not live in fear. But SARS-CoV-2 has no interest in their terror, only their cells.”

Ed Yong, The Atlantic, March 25, 2020

Where Are We Now?

- Clear that Delta is a completely different virus – all prior assumptions about the virus/vaccines need to be reassessed
- Levels of immunity that we thought would be sufficient to create herd immunity are not enough to beat back Delta
- Boosters clearly needed in highest risk groups – others still debatable
- Society’s tolerance of the unvaccinated has waned, to near-zero
- Thus enthusiasm for mandates and other sharp-elbow tactics
- “Back to normal? now impossible to predict given need to reach >85% immune for herd immunity, low vaccine rates, and waning immunity from vaccine and infection

What Will the End Game Be?

Covid-19 and the Digital Transformation of Healthcare
“I joined Mayo on January 1, 2020… and I was handed the 2030 [digital transformation] plan. Do you know that in 2020, we finished the 2030 plan?…. Covid accelerated 10 years into 10 months.”

John Halamka, MD
President, Mayo Clinic Platform
on “In the Bubble” podcast, 4/28/21

The Fundamental Question About Telemedicine/Virtual Visits

► Is it simply a visit replacement?
  - Fine if so: convenient for patients, maybe for providers
  - Opens up new non-geographically-determined care options
  - Potentially good for patients, but new competitive threats for health systems

► Or does it pave the way for true virtual care – the real game-changer?
  - Patients no longer coming into office to get BP, weight, glucose checks, etc. means new dependence on digital data streams
  - Measures less episodic; more semi-continuous
  - The trillion-dollar question: how will we manage these new data flows?

Patient 112’s sugar is high again: the algorithm bumped the insulin but let’s get the coach involved

Patient 13’s weight is up and O2 sat is worse. I’ll lock the salt shaker and the fridge

Patient 42 has irregular HR and is short of breath. Let’s do a televisit ASAP

The Care Traffic Controllers
Dashboards

Finally (!)… taking all that data and delivering usable, real-time information in visually attractive and actionable form to managers and clinicians.
How About AI and Interoperability?

While one might have anticipated the pandemic would be a moment for AI to shine, I can’t identify a true game-changing AI application.

The pandemic exposed our lack of digital connectedness; in 2020-21, we still found ourselves faxing spreadsheets.

Health IT Needs Its Golden Spike
“Maybe the Stupidest Thing I Ever Said to a Mentee”

“What will you do after we’ve implemented our EHR?”

Digital Health Investments Accelerating

Why Health IT May Finally Be Entering a New (Post-EHR) Phase

Winners in EHR derby: healthcare-specific companies, good at collecting data & moving it around

They were ready when healthcare went digital

Not expert in consumer-facing tools, user interface, data visualization, learning from data, communication,…

Now entering the post-EHR era, facilitated by value pressure, more interoperability, labor shortages and the overwhelming problem of the in-box, AI, digital companies maturing,… and the obvious limitations of what EHRs can offer

Healthcare organizations are going to need to remake themselves to thrive in this era
Managing the Post-EHR Era: UCSF’s New Digital Org Chart

“Traditional” Digital Arm

- Solving core clinical and business problems
- Focused on EHR and related tools

Digital Solutions Shop

- Solving big, hairy problems
- Longer time horizon w/o single/simple solution
- Use of diverse tools

Integration

Several Easy Predictions, and a Hard One

- Health IT will, ultimately, transform and disrupt health and healthcare
- Covid has shortened the timeline for this by several years
- The new system will be less institution-focused, less geographically determined, more patient-centric, and deliver higher quality, less expensive, and more equitable care
- The winners will be any one of these four parties:
  - Existing healthcare organizations that thoughtfully embrace transformation
  - EHR vendors that innovate and open their architecture
  - Digital giants that are able to maintain a focus on health (lower probability)
  - New companies (start-ups) that skillfully address important use-cases
- The hard thing to predict: when?

“In theory there is no difference between theory and practice. In practice there is.”
- Yogi Berra (maybe)
Case #1

- A 67F is hospitalized with a community-acquired pneumonia. On Day #3 she is feeling much better awaiting discharge when her nurse finds her unresponsive with rhythmic shaking of all limbs.
- PMHx: COPD
- Meds: Ceftriaxone, NKDA
- SH: 100pk yr hx tobacco, no hx EtOH
- FH: No neurologic disease

Case #1

- You are called to the bedside and after 3 minutes, these movements have not stopped. Options for your next course of action are:
  A. Continue to wait for the spell to subside
  B. Administer IV Diazepam
  C. Administer IV Lorazepam
  D. Administer IV Fosphenytoin

Case #1

- Following Lorazepam 2mg IV x 3 (2 minutes apart), the patient is still having these movements (now 7 minutes). What is your next course of action?
Status Epilepticus

- Changing definition and time window
- Incidence: 100,000 to 150,000 per year nationally
- Contributes to 55,000 deaths per year nationally
- 12 to 30 percent of epilepsy first presents as status
- Generalized convulsive status most dangerous

Status Epilepticus Algorithm: Real World

1. Lorazepam 2mg IV q2 minutes up to 6-8mg or Midazolam 10mg IM*
2. Fosphenytoin 18-20mg/kg (Dilantin Equivalents) IV**
3. General Anesthesia with continuous EEG
   a. IV Midazolam gtt
   b. IV Propofol gtt

Recent Large Trial

IM Midazolam: RAMPART

- Out of hospital non-inferiority trial
  – 4 mg lorazepam IV vs. 10 mg midazolam IM (the latter using a novel autoinjector)
- Primary outcome: absence of sz at time of ED arrival without the need for rescue therapy

Which to Choose After Benzos: ESETT Trial

- After benzos, if still; seizing randomize to:
  - IV Fosphenytoin, Valproate, or Levetiracetam
- Primary outcome was cessation of status and improvement in mental state at 60 min


Seizure Management: Once the Spell Stops

- Key Question:
  - 1st seizure or known epilepsy

Seizure Management: First Seizure

- Careful history of the spell: before (including recent events), during, after
- Determine all meds patient is on
- Careful neuro exam looking for focal signs
  - Focal exam= Partial seizure= Focal lesion

Seizure Management: First Seizure

- Work-up for provokers
  - Head trauma?
  - Utox, EtOH history and possible level
  - CBC, Lytes, Ca/Mg/Phos, BUN/Cr, LFTs
  - CT (usually with contrast)
  - Very low threshold to LP
- Needs outpatient work up including: EEG, MRI, and neurologic consultation
Seizure Management: Known Epilepsy

• 1. Non-compliance
  – Determine AEDs including doses
  – Send levels of AEDs if possible
  – Med-Med interactions
• 2. Infection
  – CXR, urine, blood cx, consider LP
• Best to curbside primary neurologist regarding any medication changes to current regimen

Case #2

• A 50 year-old man is brought in to the ED by his girlfriend with several days of paranoia and unusually aggressive behavior.
• General physical exam is normal. Neurologic examination shows a disoriented man threatening the staff
• Labs: Lytes, CBC, BUN/Cr, LFTs, Utox all nl
• CT head negative, CXR negative, U/A negative

What is the next test you would like to order?

A. MRI Brain
B. LP
C. Blood Cultures
D. Urinary Porphyrins
E. EEG

Lumbar Puncture

• Opening Pressure 19 cm H₂O
• 18 WBCs (94% Lymphocytes)
• CSF Protein 58
• CSF Glucose 70
• Gram stain negative

• Empiric treatment begun
**HSV-1 Meningoencephalitis**

- **Diagnosis**
  - CSF lymphocytic pleocytosis (can be normal)
  - EEG (can be normal)
  - MRI (can be normal)
  - CSF HSV PCR
- If suspected, start IV acyclovir 10-15mg/kg q 8 hours

**Meningitis Treatment by the Neurologist**

- Perform LP immediately after imaging if any CSF infection suspected
- **Empiric Bacterial Treatment**
  - Vanco 1 gram IV q6-8 hrs
  - CTX 2 grams IV q12 hrs
  - Amp 2 grams IV q4 hrs (if immunosup., >60)
  - Dexamethasone 10mg IV q6

**Treatable Causes of a Lymphocytic Pleocytosis**

- **Viral**
  - Acute HIV
  - HSV, VZV
  - CMV
- **Bacterial**
  - Syphilis
  - Lyme
  - Leptospirosis

**Treatable Causes of a Lymphocytic Pleocytosis**

- **Fungal**
- **TB**
- **Neoplastic**
- Incompletely treated bacterial meningitis
- **Parameningeal Focus**
Case #3

• A 63yo man comes to the ED with 3 days of inability to walk. The patient reports a 2 week history of tingling in his hands and feet while also stating that he has been stumbling while walking for five days.

Case #3

• Exam
  – General exam nl with stable vitals
  – Mental status, cranial nerves normal
  – Motor exam with mild-moderate symmetric weakness prox>distal in the upper ext., distal>prox in the LEs
  – Sensory exam completely normal
  – Reflexes 2+ throughout except 0 ankles, plantar response flexor bilaterally

Case #3: Additional Tests

FVC/MIF: 1.2L, -30
Lumbar Puncture: Opening pressure normal, 2 WBC, Zero RBC, Protein 102, Glucose normal

Guillain Barre Syndrome: Key Points

• Clinically must think in the setting of paresthesias and weakness
  – Normal sensory exam, weakness not always ascending
  – Areflexia the rule, but not early in the disease
  – High protein with no cells on LP the rule, but not early in the disease

• EMG/NCS for diagnosis
  – Axonal and Demyelinating forms

• Antecedent illness or infection only 30%

• Other Variants: Miller Fisher variant w/ GQ1b Ab
Guillain Barre Syndrome: Key Points

- What will kill the patient
  - Respiratory Failure: Intubate for less than 20cc/kg
  - Frequent MIF/FVC
  - ICU or stepdown care always
  - DVT/PE: SQ heparin
  - Autonomic instability: cardiac (telemetry), ileus
- Treatment
  - IVIg or Pheresis, NOT steroids
  - The earlier the better

Case #4

- A 40 yo man comes to the ED with increasing weakness and dyspnea. The patient states that he has a history of myasthenia gravis diagnosed at an OSH two weeks ago but “things are going downhill.” He is on Mestinon (pyridostigmine) 60mg PO q4hrs and Prednisone 60mg PO qd. MIF is –10, FVC 250cc

Myasthenic Crisis

- True crisis vs. cholinergic crisis
- Triggers
  - Infection, surgery, initial steroids
- Management
  - Usually stop all anti-cholinesterase meds
  - Pheresis or IVIg
  - ICU, intubation, DVT/PE prophylaxis

Myasthenia Gravis: Key Points

- Two types of myasthenia
  - Young F>M
  - Old M=F
- Diagnosis
  - Antibodies (90% in generalized myasthenia)
  - EMG with repetitive stimulation
Myasthenia Gravis: Key Points

- Management
  - Pyridostigmine (Mestinon)
  - Immunosuppression
    - Prednisone first then Imuran/CellCept/Cytoxan
  - What about the Thymus?

Case #5

- A 32M comes to the emergency room with the “worst headache of his life” for 8 hours
- Non contrast CT is normal

Which of these historical points is most useful to differentiate SAH from benign headache syndromes?

A. Associated nausea/vomiting
B. Associated photophobia
C. Severity of pain
D. Peak time to maximal pain
E. Pain location

SAH Diagnosis

- CT sensitivity greatest early
- LP sensitivity greatest late
  - What do you look for?
    - Xanthrochromia?
    - Blood that fails to clear?

First 6-8 Hours  6-8hrs to 1-2 weeks

Wijdicks 2004
SAH Treatment

• Urgent Blood Pressure Management
• Etiology
  – 1. Aneurysm
    • Need to secure with clipping or coiling ASAP
      – ISAT trial (Lancet 2005)
  – 2. Trauma

Case #6

• A 65 year-old man with a history of DM, HTN presents with 1 day of imbalance and severe vertigo
• Examination shows R>L severe ataxia of the limbs with inability to walk due to imbalance. Power is normal throughout.

Which of the following most reliably distinguishes central from peripheral vertigo?

A. Severe vomiting
B. Inability to walk
C. Inability to sit upright without falling to one side
D. Presence of nystagmus
E. Slurred speech

Case #6 (con’t)

• Patient discharged from the ED
• BIBA 24 hours later after respiratory arrest at home, now in coma
Emergent ICP Management

• Step 1: Head of bed to 30 degrees
• Step 2: Hyperventilation
  – Cerebral vasoconstriction with decreased P,CO₂
  – Onset rapid
  – Lasts only 1-2 hours as buffering occurs
• Step 3: Mannitol 1 gram/kg IV (50-100g)
  – Removes brain water
  – Tolerance develops, must follow serum osms
• Step 4: Barbiturates (bolus then infusion)
• Consider ventriculostomy if indicated!

Emergent CPP Management

Cerebral Perfusion Pressure (CPP)

CPP = MAP - ICP

Cerebellar Ischemic Stroke

• Maximal swelling: 3-5 days
• Decompression indicated if patient decompensates
• Will only see on MRI
• “Malignant Meniere’s”
Sinus pauses (and vagotonic AV block are common and usually benign)

- Sleep study?

When do you consider a pacemaker for sinus node disease?

- **SYMPTOMS**
  - Presyncope or syncope with a sinus pause > 3 seconds
    - NOTE: not JUST a sinus pause > 3 seconds
  - This does include post-conversion pauses
    - An AF ablation MAY be sufficient in those cases
  - Chronotropic incompetence
    - Need to ambulate the patient
    - May require an exercise treadmill test
    - More of a quality of life issue than a safety issue

Ms. Jones has a Pacemaker

- Do I need to have the pacemaker checked?
  - Pacemaker in place is not itself an indication for a pacemaker interrogation
    - Pacemaker interrogations drain battery
  - Can assess:
    - If the leads are working
    - Timing of various tachyarrhythmias

Ms. Jones has a Pacemaker

- The device site looks red and maybe is infected?
  - DON’T STICK A NEEDLE IN IT!
  - Device infections are a big deal
  - Can be hard to eradicate infections without removing WHOLE DEVICE
  - Chronic leads adhere to the great vessels and the heart
  - Extraction tools work well, but still high risk
  - Bacteremia plus pacemaker (or ICD) should be considered possible endocarditis
    - Low threshold to get ID and EP involved
Atrial Fibrillation

• NOACs are now DOACs (no longer novel)
• We generally UNDER-ANTICOAGULATE

In the Spirit of trying to Enhance Appropriate Anticoagulation in AF

• “Your patient never calls you in the middle of the night to thank you for not having a stroke.”
In the Spirit of trying to Enhance Appropriate Anticoagulation in AF

• “Your patient never calls you in the middle of the night to thank you for not having a stroke.”

How is This Relevant to Hospital Medicine?

• That patient who develops atrial fibrillation in the setting of cellulitis or pneumonia
  • Assume you were lucky to catch it because the patient was being monitored
  • Anticoagulate unless there is a compelling reason not to
    – Examples:
      » CHADSVASC of 0 or perhaps 1
      » History of hemorrhagic stroke

Gialdini et al. JAMA 2014

No Clinical Benefit of Warfarin in Patients With Atrial Fibrillation: A Report From the Versilch-Antithrombin Cohort Study
Leifors, Matsen, Ravnkilde and Gregory Y.H. Lip

Gialdini et al. JAMA 2014
• Multiple studies have now shown:
  - Heightened risk of dementia with AF
  - Dementia/ cognitive decline risk mitigated by anticoagulation
What about the other most commonly consumed beverage in the world?
Caffeinated could reduce AF via:
- Anti-inflammatory effects
- Anti-vagal effects
- Caffeine may prolong LA effective refractory periods

Atrial Fibrillation Ablation

- Success in 60-90%
- Overall risks (4-6%): 1-5
  - Risk of death or permanent disability <1%
- A great option for symptomatic patients
- An ELECTIVE PROCEDURE

2. JACC 2003;42:185-197
3. JACC 2004;43:2044-53
4. JAMA 2005;293:2634-40
Atrial Fibrillation Ablation

- CLASS 1 INDICATIONS:
  - Selected patients with symptomatic paroxysmal AF refractory or intolerant to at least one class I or III antiarrhythmic drug when a rhythm control strategy is desired
- CLASS III: Don’t do it to get a patient off anticoagulation

Atrioesophageal Fistula

- Presents 1-3 weeks AFTER ablation
  - Fever
  - TIA or other embolic phenomena
  - Chest pain
  - Odynophagia (but not necessarily)
  - Leukocytosis
  - Hematemesis (more rare)

Atrioesophageal Fistula

- High mortality
- Get electrophysiology involved
- Get CT surgery involved
- Diagnose with CT with intravenous and water soluble GI contrast
- DO NOT DO EGD WITH INSUFLATION
- If test negative, may need to look again
- In some cases with high suspicion, take to OR directly even with negative tests

STAF (n=200)- no difference in composite endpoint of death and thromboembolic events
PIAF (n=252)- No difference in symptomatic improvement
HOT CAFÉ (n=205)- No difference in composite death, thromboembolic events, hemorrhage
Why ever consider rhythm control?

- Unlikely to include symptomatic patients in those studies
  - Rationale for rhythm control is primarily symptoms
- Warfarin was stopped when sinus apparent
- Evidence that those in sinus lived longer
Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

- 2,789 patients with recent AF and CV co-morbidities (median 36 days) randomized to rate vs rhythm control followed median 5.1 years
- ANTICOAGULATION CONTINUED EVEN IF IN SINUS
Atrial FLUTTER

- Anticoagulation=AF
- Often difficult to rate control
  - “Decremental conduction” of the AV node
- Hard to suppress with drugs
- Easy to ablate

N=>32,000 atrial flutter patients in California over 5 years

Healthcare Utilization and Clinical Outcomes after Catheter Ablation of Atrial Flutter

- N=>32,000 atrial flutter patients in California over 5 years

Supraventricular Tachycardias
Supraventricular Tachycardias

Adenosine
• Metabolized by red blood cells and endothelium
• Give 6 mg IV with 20 cc flush
• Repeat with 12 mg IV X 2
• How do I know if I’ve given enough?

75% reduction in ED visits among those undergoing catheter ablation (p=0.003).

Avoiding Left Ventricular Dyssynchrony
• Left bundle branch block may lead to heart failure

RV Pacing Causes Left Ventricular Dyssynchrony
• We try to avoid RV pacing
• NEED to avoid RV pacing with low EF
RV Pacing Causes Left Ventricular Dyssynchrony

- We try to avoid RV pacing
- NEED to avoid RV pacing with low EF
  - Change mode to only pace in the atrium if AV conduction is intact
  - Upgrade or place a Biventricular pacemaker
  - Conduction system pacing (pacing the His or left bundle branch) is gaining in popularity

Another Cause of Left Ventricular Dyssynchrony: PVCs

- Suppression or elimination of PVCs in those with reduced EF can improve (sometimes completely) systolic dysfunction

Another Cause of Left Ventricular Dyssynchrony: PVCs

- Frequent PVCs (>5%) with low EF → refer to EP
- Symptomatic PVCs → refer to EP
- Frequent PVCs (>5%) asymptomatic and normal EF, annual echos, consider referral cardiology
Conclusions

Pacemaker for SYMPTOMATIC sinus problems

Generally leave pacemakers alone

...BUT if they are pacing in the RV all the time and have any reduced EF, let EP know!

Conclusions

Anticoagulation generally GOOD

Exercise GOOD

Alcohol BAD

Caffeine/ Coffee probably OK

Rhythm control probably PREFERRED

Conclusions

Low threshold to refer to EP

Usually fine to do upon discharge

Referral to PMD is not the same

SVT

Atrial flutter

Frequent PVCs

Thank You

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Join the Study https://www.health-eheartstudy.org/
Among 359, 315 AF patients in the NCDR PINNACLE registry, 27% of all patients with CHA₂DS₂-VASc of 0 were prescribed an anticoagulant.
Bridging
- OK to just start warfarin without heparin
- Pharmacokinetics of NOACs can be considered similar to lovenox
- On warfarin:
  - Low risk: can hold for a week
    - For NOACs, should be gone in 2 days
  - High risk (mechanical valve, prior stroke, higher CHA2DS2-VASc), can consider unfractionated or low molecular weight heparin for warfarin
  - Continue (as is done in many EP procedures)

Bridging
- On novel agent:
  - Hold for 1 day prior to the procedure (2 doses if BID, 1 dose if QD)
  - When need complete hemostasis (eg, spinal puncture, major surgery), hold for 48 hours
  - Consider continuing (as we now do in many EP procedures)

What is the first thing I need to do?
- RATE CONTROL
  - If unstable → DC shock
- Your favorite beta-blocker or calcium channel blocker
- When BP goes down:
  - Consider MORE AV nodal blockage
  - Consider Dig
  - Consider amiodarone
  - Consider esmolol
  - Consider cardioversion

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose reduction</th>
<th>Other idiosyncracies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran=Pradaxa</td>
<td>CrCl 15-30 ml/min</td>
<td>Dyspepsia ~11% (acid core)</td>
</tr>
<tr>
<td>Rivaroxaban=Xarelto</td>
<td>CrCl 15-50 ml/min</td>
<td>pK maybe really 2x day drug</td>
</tr>
<tr>
<td>Apixiban=Eliquis</td>
<td>2 out of 3: Creatinine &gt; 1.5, age &gt;80, weight &lt;60 kg</td>
<td>Might be used in hemodialysis</td>
</tr>
<tr>
<td>Edoxaban=Savaysa</td>
<td>CrCl 15-50 ml/min</td>
<td>Contraindicated if CrCl &gt; 95 ml/min Drug interactions (verapamil and droneradone increases)</td>
</tr>
</tbody>
</table>
Novel Anticoagulants

• Reversibility?

• Announcement of FDA approval 10/16/15

“Let’s just cardiovert back to sinus rhythm so we don’t need to worry about anticoagulation.”
I decide to go with

Cardioversion can reduce left atrial appendage function
  – Even from AF to sinus
• The pericardioversion period is a particularly pro-thrombotic time
  – Regardless of mode: DC/ electrical, pharmacologic, spontaneous

Prior to cardioversion:¹, ²
  – Can exclude preexisting thrombus by TEE
  – Can anticoagulate (therapeutic/for at least 3 weeks) prior to cardioversion

¹. JACC 2006;48:e149-246
². Chest 2004;126:429S-456

During and after cardioversion:¹, ²
  – Anticoagulation for at least 4 weeks
  – Applies even to those who would otherwise not require anticoagulation

¹. JACC 2006;48:e149-246
². Chest 2004;126:429S-456

Epidemiology

• AF is the most common sustained arrhythmia in adults
• Affects ~4% of everyone over age 60 and ~10% of everyone over age 80
• The age-adjusted incidence is increasing¹

¹. Miyasaka Y. Circulation 2006;114:119-125
Oncologic Emergencies in Hospital Medicine
Sam Brondfield, MD, MAEd

Disclosures
• Consulting fees:
  • Gemini Health
  • IDEO
  • American Physician Institute
  • Blackstone
  • PAI Pharmaceuticals
• Honorarium:
  • Doximity

Learning Objective
Describe inpatient management of solid tumor oncologic emergencies.

Outline
• Five cases of oncologic emergencies (4 old, 1 new)
• Review of key take-aways
Overview

Solid Tumor Oncologic Emergencies

Metabolic

Structural

Treatment-Related

Case 1

A 60 year-old man is diagnosed with metastatic small cell lung cancer, including an 8 cm hilar lung mass, mediastinal lymphadenopathy, and diffuse bone lesions. He is admitted for expedited workup. Baseline labs, including chemistries, are normal. Oncology administers inpatient carboplatin/etoposide. You ponder the risk of tumor lysis syndrome.

Which of these lab abnormalities is consistent with the pathophysiology of TLS?

A) Elevated calcium
B) Low potassium
C) Low phosphorus
D) Elevated uric acid

Tumor lysis syndrome

Cancer cell lysis

Chemo (or spontaneous)

Blood

K
Phos
Ca
UA
BP

K
Phos
DNA
Cytokines

N Engl J Med 2011;364:1844-54
**Tumor lysis syndrome**

**Cairo-Bishop Criteria for laboratory TLS (2 of 4)**

<table>
<thead>
<tr>
<th>Element</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>≥6.0 mEq/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>≤7.0 mg/dL</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>≥4.5 mg/dL</td>
</tr>
<tr>
<td>Uric acid</td>
<td>≥8.0 mg/dL</td>
</tr>
</tbody>
</table>

**Clinical TLS**

Laboratory TLS plus one of:
- Cr >1.5x ULN (or >1.2-1.3)
- Arrhythmia
- Seizure

**Or 25% change from baseline**

**Tumor lysis syndrome**

- **Step 1: Risk stratification**
  - Bulky small cell lung cancer and bulky germ cell tumors = intermediate risk
  - Other solid tumors mostly low risk
  - Check baseline TLS labs

- **Step 2: Interventions**

<table>
<thead>
<tr>
<th>Risk of Clinical TLS</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
<th>Established</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluids</td>
<td>Fluids with chemotherapy</td>
<td>4-6L/day; 100-200 cc/hr UOP</td>
<td>4-6L/day; 130-200 cc/hr UOP</td>
<td>4-6L/day; 150-200 cc/hr UOP</td>
</tr>
<tr>
<td>Allopurinol*</td>
<td>Not needed</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Rasburicase</td>
<td>Not needed</td>
<td>+/-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lab monitoring</td>
<td>Daily</td>
<td>q8-12 hrs</td>
<td>q8-16 hrs</td>
<td>q4-8 hrs</td>
</tr>
</tbody>
</table>

*Requires renal dosing if renal impairment present.

**Case Wrap-Up**

- Develops TLS 24 hrs after chemotherapy
- Fluids, allopurinol, rasburicase given
- Labs improve, discharged once normalized
- Admitted for cycle 2 of chemotherapy for TLS monitoring
- No recurrence, further cycles given as outpatient

**Tumor lysis syndrome: Your role**

- Admit patient with cancer
- Most solid tumors
- Recognize and treat TLS
- Bulky SCLC or GCT
- Fluids, allopurinol, rasburicase
- Electrolyte correction
Case 2

A 58-year-old woman with metastatic non-small cell lung cancer received carboplatin/paclitaxel and is admitted 12 days later with fever and chills. Temperature is 38.5. There are no focal infectious symptoms or signs. WBC is 1.0 and ANC is 200. CXR is normal. Cultures are drawn. She has no central line.

What empiric therapy would you start?

A) Vancomycin and piperacillin-tazobactam
B) Cefepime
C) Ceftriaxone and azithromycin
D) Levofloxacin

Neutropenic fever

- Definition: 38.3 x1 or 38.0 over 1 hour with ANC <500 (or “close”)
- Primary risk factor is type of chemotherapy
- Infectious source identified in minority of cases
- Most cases are bacterial (translocation of gut flora)
- Gram negatives, S. aureus, and enterococci cause severe illness
- S. epidermidis is a common pathogen
- Anaerobes are infrequent causes of neutropenic fever

Neutropenic fever: Treatment

- Cultures → timely antibiotics → sign/symptom-directed workup
- Empiric therapy: cefepime, pip-tazo, meropenem, (cipro/amox-clav)
  - Vanc if unstable or suspect for gram+
  - Do not broaden for persistent fever alone
- Target infection if found
- If not, continue empiric regimen until ANC >500
- G-CSF generally not recommended
- Some VERY stable patients may be treated as outpatient
Case Wrap-Up

- Cefepime started
- Fevers resolve within 72 hours
- No organism identified
- On hospital day 5, feels well, ANC 600
- Discharged without antibiotics
- G-CSF given with next cycle of chemotherapy

Neutropenic fever: Your role

Admit (usually) → Cultures and antibiotics

Find and treat standard infections

If no infection found, continue empiric therapy until ANC > 500

If condition not improving after 3-4 days → consult ID

What is the most likely cancer and mechanism of hypercalcemia in this case?

A) Parathyroid carcinoma secreting PTH
B) Lung adenocarcinoma with occult lytic bone metastases
C) Squamous cell lung cancer secreting PTHrP
D) Lymphoma causing elevated 1,25-dihydroxyvitamin D3
Hypercalcemia of malignancy

- Most common cause of hypercalcemia in hospitalized patients
- Most common causes: breast, lung, renal, myeloma
- Workup: PTHrP, vit D, imaging, +/- SPEP
- Indications to treat: Ca>14 (albumin corrected), symptoms, or fast rise

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTHrP</td>
<td>80%</td>
</tr>
<tr>
<td>Osteolytic lesions</td>
<td>20%</td>
</tr>
<tr>
<td>1,25-dihydroxyvitamin D</td>
<td>Rare</td>
</tr>
<tr>
<td>PTH</td>
<td>Very rare</td>
</tr>
</tbody>
</table>


Hypercalcemia of malignancy: Management

- Dialysis (for transfers)
- Isotonic fluid 200-300 cc/hr (if Cr<4.5)
- Zoledronate 4 mg IV x1 (Cr>4.5)
- Prednisone (symptoms only)
- Calcitonin 4-8 IU/kg q12 hrs x 48 hrs
- Prednisone (lymphoma only)
- Denosumab (Cr>4.5)
- Diuretics (only if volume overload)
- Dialysis (last resort)
- Prednisone (lymphoma only)

Hypercalcemia of malignancy: Your role

- Triage based on severity (level, pace, symptoms)
- PTH, PTHrP +/- SPEP/SFEC imaging
- Isotonic fluid Calcium Zoledronate

Case Wrap-Up

- PTHrP elevated
- Fluids, calcitonin, and zoledronate given
- Calcium improves, mental status follows
- Liver biopsy shows squamous cell carcinoma
- Discharged with outpatient oncology appointment
Case 4

A 65 year-old woman with newly diagnosed triple-negative breast cancer with diffuse spine metastases not yet on treatment presents to the ED with two weeks of progressive back pain, 24 hours of bilateral leg weakness, and urinary incontinence. MRI shows a T10 lesion causing cord compression. Performance status is otherwise excellent.

What is the next step in management?

A) Glucocorticoids
B) Urgent radiation
C) Surgical resection
D) Urgent systemic cancer therapy

Neoplastic epidural spinal cord compression

- Back pain may precede neurologic changes by weeks
- Thoracic spine most common site
- Obtain whole spine imaging (MRI)
- 10 mg IV dexamethasone x1, then 4q6 IV or PO
- Caution if lymphoma on dx
- Surgery vs XRT depends on severity, radiosensitivity, and prognosis
- Radiosensitive: lymphoma, myeloma, testicular seminoma

Case Wrap-Up

- Dexamethasone started
- Laminectomy and fusion performed
- Steroids tapered over four weeks, recovers well
- Sees oncology to start systemic therapy

N Engl J Med 2017;376:1358-1369
Neoplastic epidural spinal cord compression: Your role

MRI total spine w/ contrast → Give dex 10 mg IV, then 4 mg PO q6 hrs → Call neurosurgery and radiation oncology

Case 5

A 60 year-old man with metastatic melanoma and no other comorbidities who started ipilimumab and nivolumab 3 months ago presents with subacute progressive dyspnea. CT shows shrinkage in all metastatic lesions and new diffuse ground glass opacities in both lungs. He is afebrile. Hypoxemia progresses rapidly requiring intubation. Exam shows diffuse inspiratory crackles and flat JVP. Pulmonology performs BAL with results pending. Broad-spectrum antibiotics are started.

What is the next step in management?

A) Switch to oral ipilimumab/nivolumab
B) Start oral prednisone
C) Start IV methylprednisolone
D) Start IVIG and infliximab

Brief Overview of Immune-Related Adverse Events (IRAEs)

- IRAE = inflammatory side effect
- Occur weeks to months after initiation of checkpoint inhibitor
- Variable severity
- Can affect any organ system
- Some are “emergencies” (prompt attention to avoid bad outcome)
Severe IRAE Treatment Approaches

- Rule out other causes (e.g. BAL)
- Consult organ-specific specialist
- For most severe IRAEs, IV steroids are first step
- Additional immunosuppression if no improvement in 48 hrs

Case Wrap-Up

- IV methylprednisolone 2 mg/kg started
- Infectious workup returns negative
- Oxygen requirement decreases
- Steroids tapered over 6 weeks as outpatient
- Immunotherapy discontinued permanently

Severe IRAE: Your role

Review of key take-aways
Tumor lysis syndrome: Your role

Admit patient with cancer

Most solid tumors

Bulky SCLC or GCT

Recognition and treat rare cases of TLS

Fluids

Allopurinol +/- Rasburicase

Electrolyte correction

Neutropenic fever: Your role

Admit (usually)

Cultures and antibiotics

Find and treat standard infections

If no infection found, continue empiric therapy until ANC > 500

ID consult if condition not improving after 3-5 days

Hypercalcemia of malignancy: Your role

Triage based on severity (level, pace, symptoms)

PTH

PTHrP

vit D +/- SPEP/SFLC

Imaging

Isotonic fluid

Calcitonin

Zoledronate

Neoplastic epidural spinal cord compression: Your role

MRI total spine w/ or w/o contrast

Give dex 10 mg IV, then 6 mg PO q 6 hrs, pain control

Call neurosurgery and radiation oncology
Severe IRAE: Your role

- Rule out other causes (infection)
- Consult organ-specific specialist
- IV steroids typically first line

Thanks!
sam.brondfield@ucsf.edu
UCSF Management of the Hospitalized Patient
October 2021

Year in Review
Brad Sharpe, MD
Brad Monash, MD

The Year in Review will highlight key articles from the last year in the field of hospital medicine, from September 2020 to September 2021. Articles were selected based on article quality and ability to impact and change practice. We will not be presenting articles related to COVID.

The articles will be presented in an interactive case-based format as we will follow a few patients through their hospital stay.

In order to avoid duplicating articles of other speakers, we are in the final stages of selecting the articles and a version of the slides will be posted ahead of the conference.