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Hospitalist Updates:

Tick Borne Illness in Missouri

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Missouri is a hotbed for tick-borne illness given its abundance of rural geography and wildlife, especially deer. The two most frequently encountered ticks in Missouri are the lone star tick, *Amblyomma americanum* and the American dog tick, *Dermacentor variabilis*. Amblyomma related diseases in Missouri include human monocytic ehrlichiosis, Rocky Mountain Spotted Fever (RMSF), Southern Tick-Associated Rash and Illness (STARI), Tularemia, and Heartland Virus. Dermacentor ticks are capable of transmitting RMSF and Tularemia.

Approximately 40% of all tularemia cases reported to CDC each year occur in Arkansas, Oklahoma, and Missouri.(1) Through 2000-2007, 190 cases of Tularemia were reported in Missouri, for an annual incidence of 4 cases per million population, accounting for about 20% of all cases annually nationwide. The infecting

agent, *Fransisella tularensis*, is highly contagious and is considered an agent of bioterrorism. The presentation of tularemia depends on the mode of acquisition. A tick bite usually leads to an ulceroglandular presentation, the most common presentation. The disease can also be contracted through contact with infected animal tissues, eating contaminated food or water, or inhalation of contaminated aerosols. Typically an ulcer appears at the point of the organism's entry with regional adenopathy developing; sometimes an ulcer is not found, though. Inhalation can lead to pneumonia and/or a typhoidal-like systemic illness. An oculoglandular presentation has been seen in microbiology lab workers handling live cultures. An oropharyngeal presentation manifests with neck adenopathy. The majority of patients give a history of fever. A pneumonic presentation usually shows a leukocytosis, but this is usually absent in other presentations. Glandular presentations are frequently misdiagnosed as other more common glandular diseases such as gram-positive lymphadenitis, cat scratch disease, and Epstein-Barr virus infection. Pneumonic presentations are usually diagnosed and treated initially as community-acquired pneumonia. The clinical diagnosis is confirmed by a 4-fold rise in antibody titer between acute and convalescent serum samples taken at least two weeks apart; culture; or by PCR which is not readily available. FDA-approved antimicrobials include tetracyclines and aminoglycosides. Tetracyclines should be given for at least 14 days. Ciprofloxacin for $\geq$ 10 days has shown a 90% success rate for treatment.(2, 3)

In 2011, Missouri practitioners identified 270 confirmed and probable cases of RMSF. This count translates to a statewide incidence rate of 4.5 per 100,000, making it Missouri's most common tick-borne disease. *Rickettsia rickettsii,* the infecting agent, is transmitted to the victim 6-10 hours after tick attachment, and the first symptoms usually begin 2-14 days after the tick bite. Patients with RMSF typically seek care in the first 2-4 days of illness; symptoms include sudden high fever, shaking chills, severe headache, muscle aches, and joint pain. Children sometimes suffer from nausea, vomiting, and a loss of appetite. The classic spotted rash of *R. rickettsii* infection is usually not apparent until the fifth or sixth day of illness and is not observed in all people. The rash has been mistaken for the rash of meningococcal septicemia. Additional diagnostic clues can include a low platelet count, low sodium levels, or elevated liver enzyme levels. Antibodies to *R. rickettsii* are detectable 7–10 days after illness onset. The gold-standard serologic test looks for a four-fold change in antibody titers using immunofluorescence assay (IFA) on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later. IgM antibodies are less specific than IgG antibodies and are more likely to generate false positives. IgM results alone should not be used for laboratory diagnosis. Antibody titers are frequently negative in the first 7–10 days of illness, thus serologic tests may be falsely negative during this time period. The infecting organism can also be detected by PCR of a biopsy of the rash. PCR is generally unreliable for acute blood samples. The organism can also be seen in tissues samples via immunohistochemical staining. First-line RMSF treatment for adults and children of any age is doxycycline. Treatment should continue for at least 3 days after defervescence and until the patient clinically improves. The minimum duration of therapy is 5-7 days. Fatalities from RMSF are often attributed to delays in diagnosis and inappropriate treatment.(3, 4)

In 2009, Missouri identified 167 cases of ehrlichiosis. The incidence of ehrlichiosis in men was about twice that of women, with 3.7 reported illnesses per 100,000 men compared with 2 cases per 100,000 in women. In1 to 14 days after the infecting agent, *Ehrlichia chaffeensis*, is transmitted to the host, symptoms of fever and headache usually develop. Chills, malaise, muscle pains, gastrointestinal symptoms and central nervous system manifestations may also be seen. Rash may be present in a

minority of infected adult patients. Prolonged (>2weeks) fever has been described from the patient not seeking care, the practitioner not recognizing the disease, or both. Common lab abnormalities include leukopenia with lymphopenia, thrombocytopenia, and elevated liver function tests. With proper antibiotic therapy a profound lymphocytosis has been described. Antibodies to *E. chaffeensis* are detectable 7–10 days after illness onset. The gold-standard serologic test looks for a four-fold change in IgG-specific antibody titers using IFA on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later. *E. chaffeensis* DNA can be detected by PCR on whole blood. This method is most sensitive within the first week of illness and may decrease in sensitivity after administration of antibiotics. During the acute stage of illness, morulae, or cytoplasmic inclusion bodies, may be detected in about 20% of patients, most commonly in their monocytes. Doxycycline is the preferred therapy and should be given for at least 3 days after the fever subsides and until there is evidence of clinical improvement. The minimum course of treatment is 5–7 days. Rifampin has been used successfully in pregnancy with no apparent ill effects to the newborns.(3-7)

The Lone Star tick (*Amblyomma americanum*) is the vector of Lyme-like illness, also known as STARI or Masters Disease. The causative agent is not known at this time. An erythema migrans (EM)-like lesion is seen in these patients, usually without any accompanying symptoms. When compared to Lyme disease patients, STARI patients have fewer and smaller EM lesions which are more circular and more likely to have central clearing. It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians will often treat patients with oral antibiotics.(8, 9)

There have been 2 patients to date from Missouri who have been thought to be infected with the Heartland Virus. They presented with fever, fatigue, diarrhea, thrombocytopenia, and leukopenia, and both had been bitten by ticks 5 to 7 days before the onset of illness. *E. chaffeensis* was suspected as the causal agent but was not found on serologic analysis, PCR assay, or cell culture. Electron microscopy revealed viruses consistent with members of the Bunyaviridae family. Next-generation sequencing and phylogenetic analysis identified the viruses as novel members of the phlebovirus genus. The virus has been recently detected in in nymphal *A. americanum* ticks from Missouri. The disease is most closely related to Severe Fever with Thrombocytopenia Syndrome Virus infection, transmitted by *Haemaphysalis longicornis* ticks in China and Japan, where it has a 2-15% fatality rate. There is currently no readily available diagnostic test nor specific therapy for Heartland Virus infection.(10, 11)

Other rarely seen tick-borne diseases in Missouri include Q fever from *Coxiella burnetti* and Babesiosis. I have yet to recognize a case of Lyme disease acquired in Missouri.

Prevention of tick-borne disease can easily be done using repellent containing at least 20% DEET or permethrin-treated clothing; checking oneself for ticks daily and showering soon after being outdoors; and treating dogs for ticks. Embedded ticks should be removed with fine-tipped tweezers grasping the tick as close to the skin's surface as possible. The tick should be pulled upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. If this happens, remove the mouth-parts with clean tweezers. If one is unable to remove the mouth parts easily, leave them alone and let the skin heal. After removing the tick, thoroughly clean the bite area and hands with rubbing alcohol, an iodine scrub, or soap and water.

Antibiotic treatment following a tick bite is not recommended as a means to prevent ehrlichiosis, babesiosis or RMSF. There is no evidence this practice is effective, and it may simply delay onset of disease. Instead, persons who experience a tick bite should be alert for symptoms suggestive of tick-borne illness and consult a physician if fever, rash, or other symptoms of concern develop. Tularemia prophylaxis is recommended only in cases of laboratory exposure to infectious materials. Doxycycline is generally recommended for prophylaxis in adults. Ciprofloxacin is not FDA-approved for prophylaxis of tularemia but has demonstrated efficacy in various studies, and may be an alternative for patients unable to take doxycycline.(3)

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Blood Pressure (BP) Measurements in Adults

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Uncontrolled high blood pressure is present in every 3rd person in the American community and is attributed to be a major risk factor for progression of chronic kidney disease, coronary artery disease, and stroke. Therefore, blood pressure recording is the most common measurements at home and by healthcare professionals in all of clinical medicine. It might come as a surprise that majority of recordings are done in a less than ideal circumstances and consequently performed inaccurately.

BP measurements using mercury sphygmomanometer by a trained health care professional is the gold standard for clinical assessment of blood pressures. The appearance of the 1st Korotkoff sound signals the systolic blood pressure and the disappearance of the 5th sound denotes the diastolic blood pressure. The hypertension experts believe and have increasing evidence to suggest that this method frequently either over diagnose hypertension or fail to recognize masked hypertension (blood pressure that is normal in the physician's office setting but high at other times including at home). The four commonly recognized reasons for this are:

- Avoidable inaccuracies in the methods,
- The inherent variability of blood pressure; and
- The tendency for blood pressure to increase in the presence of a health care professional (the so-called white coat effect).
- Failure to standardize blood pressure measurement dos and don'ts.

It is believed and also to some extent evidence based that the health care providers including physicians often do not follow established guidelines for blood pressure measurement. It is also suggested that when BP measurements are taken as it should be, clinic readings correlate much more closely with the objective blood pressure measures. Unfortunately, busy office or clinic readings are a very poor reflection of true blood pressures, not only because of the lack of standardization and inaccuracies of measurement technique but also because of minute to minute variability of blood pressure, a small number of readings only provides a crude estimate of the average BP.

For accurate interpretation of blood pressure readings, one needs to be aware of following issues with blood pressures:

- Diurnal variation
- Transient changes due to stressors and/or extraneous factors
- The sustained average blood pressure, what we call as hypertension that is associated with morbid events
- Non-dippers, whose pressure remains high at night are at greater risk for cardiovascular morbidity than dippers

JNC 7 classification of blood pressure is given in table 1 below.

BP Classification	SBP mm Hg*	DBP mm Hg*
Normal	<120	<80
Prehypertensive	120–139	80–89
Stage 1 hypertension	140–159	90–99
Stage 2 hypertension	≥160	1≥100

In this write up I will discuss the issues that relates to devices used for measuring blood pressure. In subsequent write ups, other issues will be discussed.

Blood Pressure Measurement Devices

1. Auscultatory method (Mercury, and Aneroid)
2. Oscillometric automated devices Technique

This method was first discovered by Korotkoff in 1905 and is still being used for measuring blood pressure. A cuff is inserted over the upper arm. The cuff is inflated such that the pressure reaches over the systolic pressure to occlude the artery. At this time the pulse over the artery disappears. The next step is to gradually deflate the cuff to reestablish the pulsatile blood flow. This is ascertained by listening to the start of the Korortkoff sound through the bell of a stethoscope placed right over the brachial artery just below the lower edge of the cuff, which typically is close to the bend of the elbow. When the sound is first heard, it is the systolic pressure. As the deflation of cuff continues, the sound becomes louder, and then gradually diminishes to a very weekend sound. Approximately 5 to 10 mm later, the sound altogether disappears. The diastolic pressure is when the sound suddenly disappears, not the point at which the sounds become weaker.

The Korotkoff sounds have been classified as having 5 phases:

1.Phase I - appearance of clear sounds corresponding to the appearance of a palpable pulse
2.Phase II - sounds become softer and longer
3.Phase III - sounds become crisper and louder
4.Phase IV - sounds become muffled and softer
5.Phase V - sounds disappear completely. The fifth phase is recorded as the last audible sound.

A combination of turbulent blood flow and the arterial wall oscillations create sounds. There is no disagreement that in the auscultatory method, the onset of phase I corresponds to the systolic pressure and even after realizing that this method tends to underestimate the systolic pressure compared to direct intra-arterial measurement. For a long time in the past, some experts considered weakening or muffling of sounds (phase IV) corresponded to diastolic pressure. But, based on diastolic pressures determined by direct intra-arterial measurements, the true diastolic pressure occurs after the complete disappearance of sounds (phase 5). Now the general consensus is to use the fifth phase as depicting diastolic pressure. Nevertheless, this approach cannot be reliably used for situations of high output states where the sounds do not disappear even until zero, like the example of blood pressures in pregnant women, patients on hemodialysis with A-V fistulas, valvular leaks such as aortic regurgitation. It is reassuring to know that most major clinical trials have been conducted using phase 5 as the diastolic blood pressure. Nevertheless, it is apparent that compared to direct measurement of intra-arterial pressures, the auscultatory method tends to give values for systolic

pressure that are lower and the diastolic values that are higher.

The mercury sphygmomanometer has always been regarded as the gold standard for clinical measurement of blood pressure. Because of the concerns of mercury exposure, use of mercury sphygmomanometer has significantly declined in the past decade.

The aneroid instrument is composed of a mechanical system of metal bellows that responds to cuff pressure and a series of levers that register pressures on a circular scale. Because of complex design, mechanical failure and aging of parts result in failure to maintain its stability over time. Therefore, these instruments tend to be less accurate over time than mercury sphygmomanometers. Moreover, they require frequent calibrations. Recent technological advances appear to overcome some of the earlier deficiencies.

The Oscillometric Technique:

This technique was first demonstrated by Marey in 1876. In later years, further advances in this area demonstrated that when the oscillations of pressure in a sphygmomanometer cuff are recorded during gradual deflation, the point of maximal oscillation corresponds to the mean intra-arterial pressure. As we know, the oscillations begin above systolic pressure and continue below diastolic. In the design of instruments, the systolic and diastolic pressures are estimated indirectly by an empirically derived equation. In this technique it is not necessary to place any device over the brachial artery. The oscillatory recordings are devoid of external sound interference. The most devices are user-friendly and require no special training in using them.

The major concerns with the technique are:

1. The influence of factors other than blood pressure on amplitude of the oscillations. This is especially a concern in elderly who tend to have stiff arteries and wide pulse pressures. In such cases, the equations that are used to estimate systolic and diastolic pressures by necessity have to be different than the one used in younger individuals. Consequently, the mean arterial pressure may be calculated lower than the true intra-arterial pressures and could easily introduce inaccuracies in the recording of blood pressures.
2. In those with considerable movement artifact, such as individuals with tremors, during physical activities, these devices are not reliable.
3. It is said the cuffs deflate at a manufacturer-specific "bleed rate" and is inflexible and matched to an assumed fixed regular pulse. These assumptions are incorporated in the equation used to determine systolic and diastolic pressure in individuals with severe tachycardia.

However, studies comparing these devices with intra-arterial and Korotkoff sound measurements have shown close agreements. Despite the concerns raised above, devices based on the oscillometric technique have been used extensively for home monitor and 24-hour ambulatory monitor. Oscillometric devices are also used now in a clinic setting.

CASE REPORT:

SENSORY-ONLY GUILLAIN-BARRÉ SYNDROME ASSOCIATED WITH COXSACKIEVIRUS B4 INFECTION

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INTRODUCTION

Guillain-Barré syndrome (GBS) is classically defined as a disorder of motor neurons but several variants that include sensory deficits have also been described. Variants that are primarily sensory, with little to no motor dysfunction, have been reported rarely. In most cases, an antecedent infection is identified. Here we present a case of sensory-only GBS associated with coxsackie virus B4 infection in a 79 year-old male. There have been rare reports of coxsackie viruses causing classic GBS or peripheral neuropathy, but to our knowledge this is the first reported association with sensory-only GBS.

CASE REPORT

A 79 year-old male presented to the emergency department in August 2013 with a one-week history of fever, chills, generalized myalgia's, and a maculopapular rash on his trunk and upper and lower extremities (Fig 1). He was febrile (38.6°C) and tachycardic (109 bpm). Laboratory studies showed leukopenia (3,400 WBC/μL) and elevated liver enzymes (AST of 101 U/L, ALT of 191 U/L). He was suspected of having a tick-borne illness such as ehrlichiosis or Rocky Mountain spotted fever (RMSF) and was started on a ten-day course of doxycycline. He showed clinical improvement and was discharged after three days. Ehrlichia PCR and RMSF antibody titers drawn at admission were subsequently found to be negative.

Four days later he returned to the ED with worsening unsteadiness which he described as difficulty coordinating his hands and feet. Physical examination revealed dysmetria, dysdiadochokinesia, and gait ataxia. Vibration sense was absent in his lower extremities as well as distal to and including his proximal interphalangeal joints. Bilateral Achilles reflexes and his left patellar reflex were absent. Strength was 5/5 in all extremities and light touch and pinprick sensation were preserved. He was oriented and had no memory deficits.

Laboratory studies revealed hyponatremia (120 mmol/L). The patient's white blood cell count had normalized since his first admission and his liver enzymes were trending downward. A lumbar puncture showed mildly elevated protein (58 mg/dL) and glucose (82 mg/dL) in his cerebrospinal fluid. A head CT scan was negative for any acute changes. Electromyography revealed a sensory neuropathy involving both the upper and lower extremities with preserved motor function. There was no evidence of axonal damage or neuromuscular junction dysfunction.

Many tests trying to determine the etiology of his neurological symptoms were ordered. Infectious agents assessed for included HSV, *Burellia burgdorferi*, *Mycoplasma pneumoniae*, VZV, HIV, syphilis, EBV, CMV, hepatitis viruses, West Nile virus, coxsackie viruses, echoviruses, adenoviruses, and repeat RMSF titers. Other tests evaluated TSH, folate, vitamin E, ceruloplasmin, a paraneoplastic panel, and a GBS-associated antibodies panel.

The patient's neurological symptoms failed to improve after correction of his hyponatremia. Given his neurological deficits following an acute, likely infectious illness, the patient was presumed to have a sensory-only variant of GBS. He was started on a five-day course of IV immune globulin IVIg) therapy. His dysmetria and dysdiadochokinesia showed improvement, and he was discharged after two weeks in the hospital to a rehabilitation facility.

A send-out titer for antibodies to Coxsackie virus B4 returned positive at a $\geq$ 1:640 titer (<1:10). All other previously-mentioned tests were negative or normal. As of March 2014, the patient ambulates without issue and has resumed his previously active lifestyle. His only lingering symptom is a tingling sensation he feels in his feet when he first arises in the morning.

DISCUSSION:

GBS is classically a disorder characterized by predominantly motor nerve demyelination with corresponding progressive muscle weakness. It usually follows an antecedent infection such as *Campylobacter jejuni*. However, there are well-known variants of GBS that involve autonomic, sensory, and cranial nerve pathways. Some of these have been well-characterized such as Miller-Fisher syndrome [1]. Other less-defined conditions with ataxia due to peripheral loss of proprioception have fallen under the umbrella of sensory-only GBS. Asbury put forth criteria that have since been used to define these sensory-only GBS variants [2-4]. These criteria include:

1. The onset must be rapid.
2. The distribution of neuropathic findings must be widespread and symmetrical.
3. Recovery must be complete or nearly so.
4. CSF protein should be elevated without elevation in cells (albumin-cytologic dissociation).
5. Electrodiagnostic results should be consistent with a demyelinating peripheral neuropathy.

Our patient fulfilled all of these criteria, with his neuropathy mainly affecting the large-diameter peripheral nerves involved in proprioception and vibration sense.

GBS is believed to be an autoimmune disease with evidence suggesting a molecular mimicry mechanism. Subtypes of GBS have different autoantibodies associated with them; in Miller-Fisher syndrome, antibodies to GQ1b are positive in 90% of cases [5]. Our patient did not have a positive titer for these antibodies or other antibodies associated with GBS.

Coxsackie viruses are implicated in hand-foot-and-mouth disease, viral meningitis, myocarditis, and pleurodynia. Our patient's presentation of fever, myalgia, rash, and liver enzyme elevation was more consistent with a tick-borne illness or mononucleosis, though tests for these were found to be negative. However, there is a case report of Coxsackie virus associated with a mononucleosis-like syndrome [6]. There have been reports of coxsackie viruses associated with classic GBS but to our knowledge this is the first report of Coxsackie virus associated with sensory-only GBS [7]. There is a previous report of Coxsackie virus B associated with autonomic neuropathy and some sensory impairment in a pregnant woman, but in this case the neuron damage was axonal and not demyelinating as in our case [8].

One limitation in tying Coxsackie virus B4 to this case is that only a single antibody titer was obtained weeks after the patient had his initial febrile illness. To diagnose a recent infection, ideally an acute titer is obtained at the onset of symptoms and then a convalescent titer is obtained weeks later, looking for

a several-fold rise in the titer. However, given that his titer for Coxsackie virus B4 was 64-times higher than the reference range and many other potential causes of his condition had been ruled out, Coxsackie virus is the most likely cause of his febrile illness and what provoked the development of sensory-only GBS.

CONCLUSION

This case demonstrates the importance of recognizing variant forms of GBS that include sensory deficits. The index of suspicion should be high when a patient presents with confusing sensory deficits following a recent infectious illness. Diagnosis can be made clinically by following the criteria put forth by Asbury. Prompt recognition facilitates early treatment which may hasten recovery.

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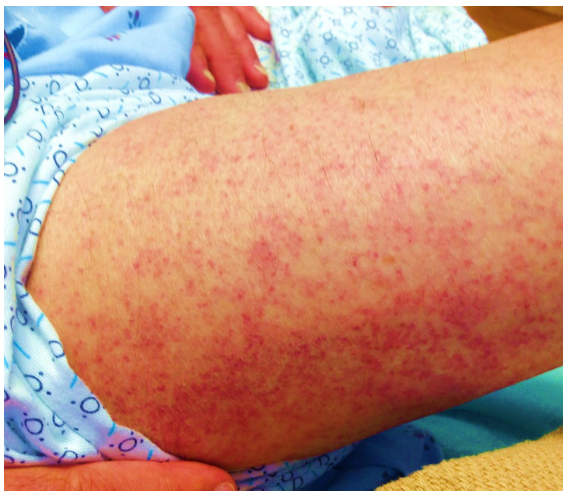

Fig 1: Maculopapular rash seen on patient's right lower extremity during his acute febrile illness.

Most Commons in Hematology and Oncology

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- Most common inherited thrombophilia: Factor V leiden —> Prothrombin gene mutation
- Most common inherited bleeding disorder: Von williebrand's disease
- Most common NHL in western world: Diffuse large B cell lymphoma (DLBCL)
- Most common malignancy in pediatric population: Acute Lymphoblastic Lymphoma (ALL)
- Leading cancers in male population in USA: Prostate cancer —> Lung cancer —> Colon cancer
- Leading cancers in female population in USA: Breast cancer —> Lung cancer —> Colon cancer
- Cancer related mortality in USA, listed in order of decreasing frequency:
  Males: Lung cancer —> Prostate cancer —> Colon cancer
  Females: Lung cancer —> Breast cancer —> Colon cancer

Useful Links and Reference:

1. http://www.cancer.org/
2. http://www.cancer.gov/
3. http://seer.cancer.gov/
4. http://ghr.nlm.nih.gov/condition/factor-v-leiden-thrombophilia
5. https://www.nhlbi.nih.gov/health/health-topics/topics/vwd/
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Diagnostic Dilemma

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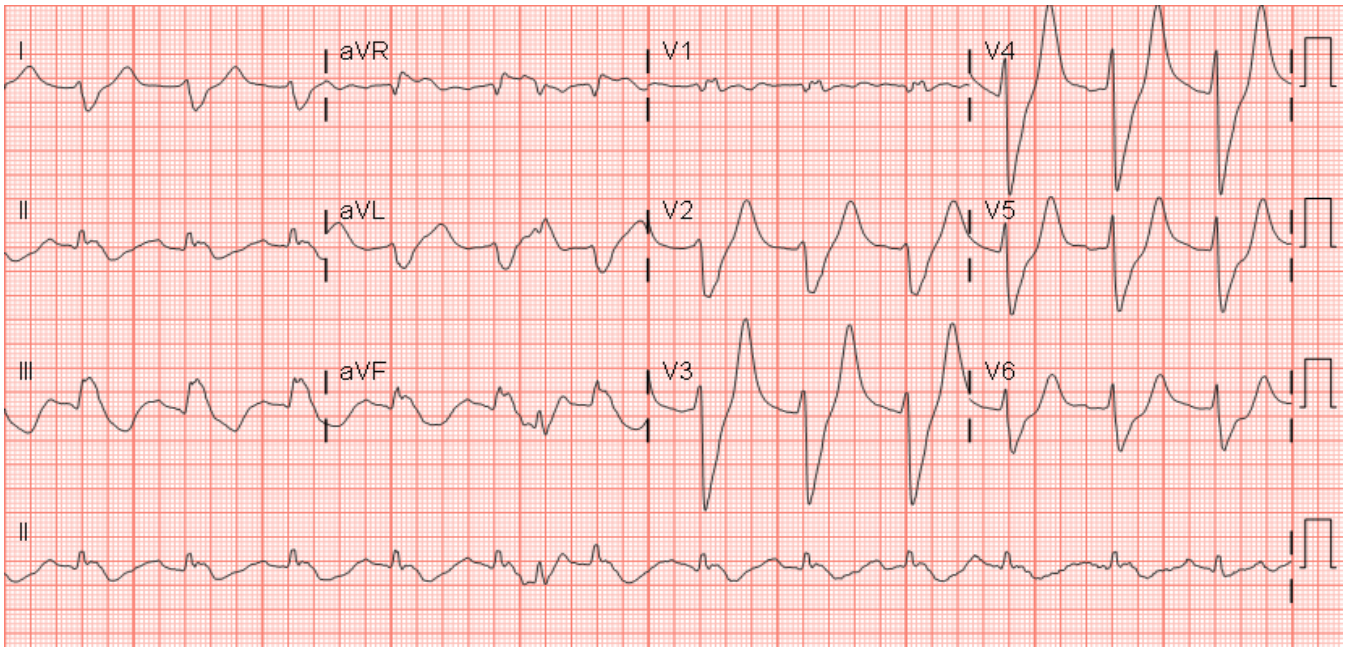
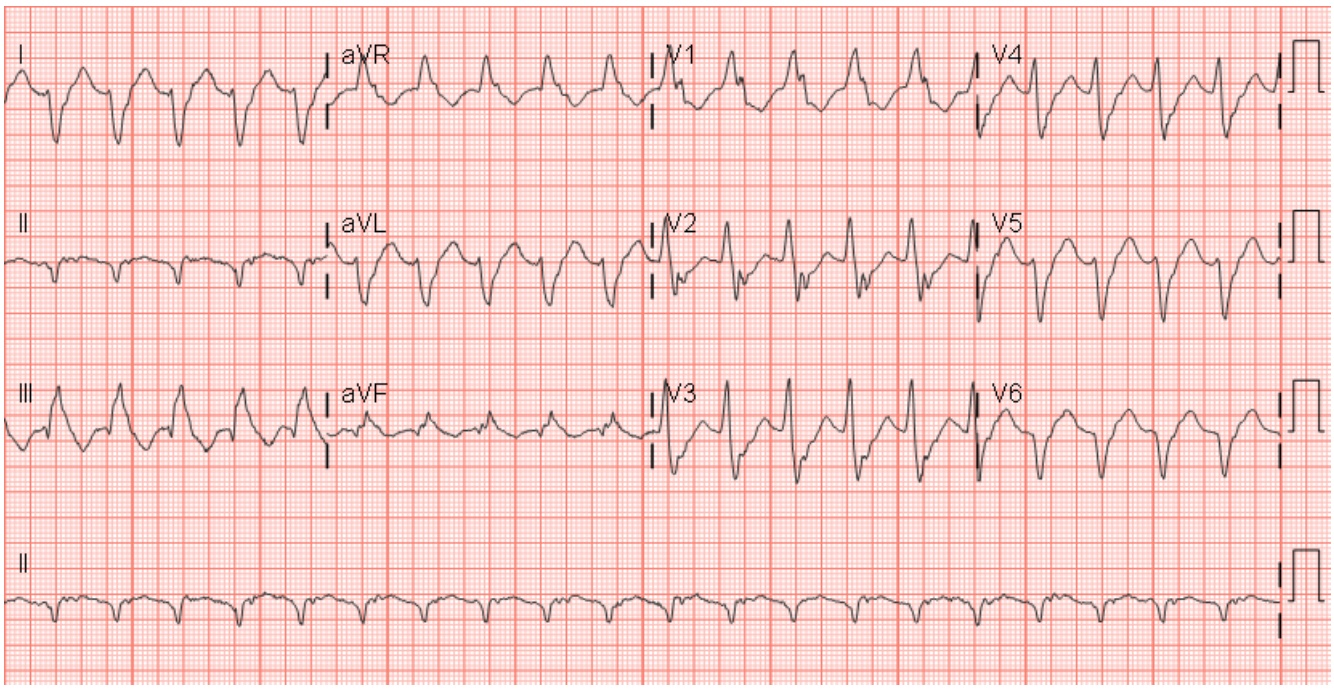
1. 40 year old African American male with history of hypertension, type 2 diabetes and ESRD is seen in the ER for symptoms of chest pain and generalized weakness. Patient is on hemodialysis for ESRD. ECG is performed in the ER and is shown below. Vitals are as follows: HR 70 bpm, BP 200/100 mm Hg RR 20/min. The next step in the management is:



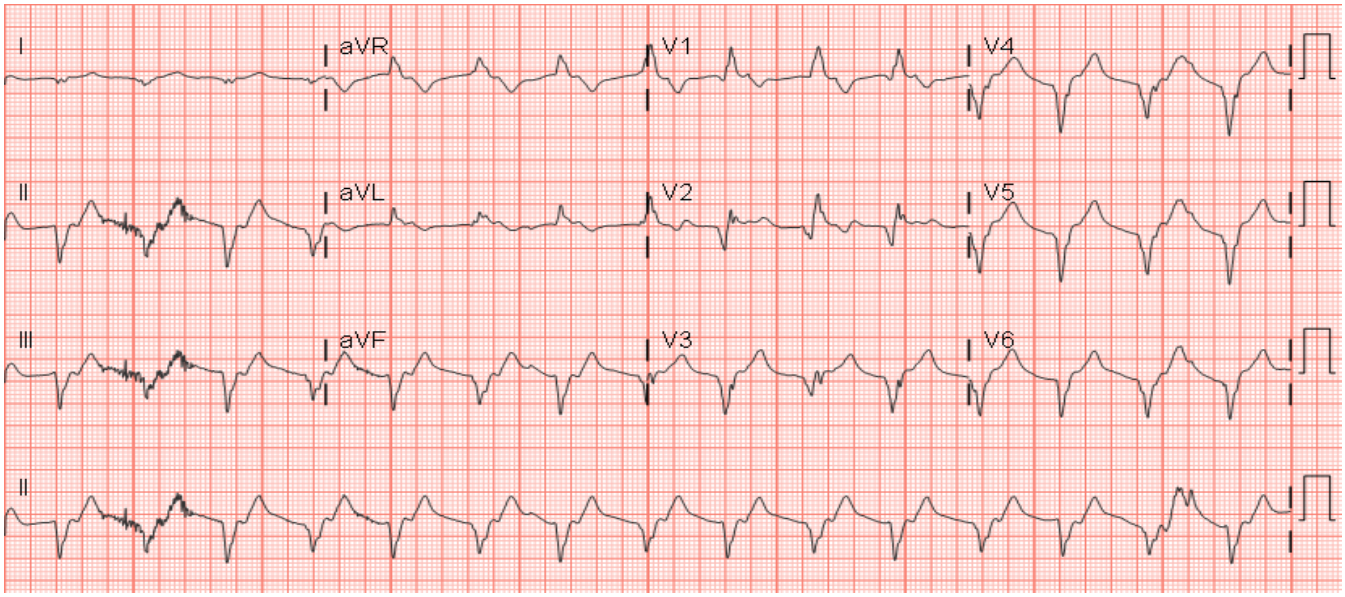
A. Start amiodarone
B. Synchronized DC cardioversion
C. No further action needed as it is a benign arrhythmia
D. Administer calcium

2. A 55 year old Caucasian female with no significant past medical history is seen in the emergency room with palpitations. She reports multiple brief episodes of palpitations both on exertion and rest over the past few months. Patient is admitted to telemetry floor. Shortly after admission she reports palpitations. A 12 lead ECG is obtained. Vital signs are as follows: HR 140 bpm, BP 80/50 mm Hg. The next step in the management of this patient is:



A. IV amiodarone 300mg bolus
B. Synchronized DC cardioversion
C. IV adenosine
D. Start diltiazem drip

3. A 56 year old Caucasian male is seen in the emergency room for an inferior ST elevation MI. He is status post emergent PCI of right coronary artery. Few hours after transfer to the ICU you are called by the nurse for the following rhythm. HR 90 bpm, BP 110/80 mm Hg. Next step in the management is



A. Administer IV lidocaine
B. Synchronized cardioversion
C. Administer IV magnesium 2 gm
D. Observation

(ANSWERS on Page 15)

ASK A PATHOLOGIST

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Question: I heard there is going to be a shortage of FFP from the American Red Cross during the next few months. What should I do when I need to urgently reverse anticoagulation in patients on warfarin?

Answer: The American Red Cross anticipates a shortage in universal donor type AB plasma (FFP or FP24) starting on April 1, 2014 because of new donor standards intended to reduce the incidence of

Transfusion Related Acute Lung Injury (TRALI). Most cases of TRALI are thought to be caused by donor antibodies directed against recipient leukocyte antigens and is associated with plasma-containing products such as FFP. Prevention of TRALI involves donor antibody testing and deferral of high-risk donors. The new donor standards are expected to decrease available universal donor AB plasma by about one-third for the next several months. Other types of plasma (A, B, O) should not be affected by the shortage, since the new standards are already in effect for these blood types.

FFP has been a mainstay for urgent reversal of anticoagulation due to warfarin. One unit of FFP (250cc) is derived from a single donor and contains all clotting factors (pro- and anticoagulant) as well as approximately 400-500mg of fibrinogen.[1] Because it also contains donor ABO antibodies, FFP must be ABO-compatible. The most common adverse reactions include transfusion reactions and Transfusion Associated Volume Overload (TACO).

In 2013, the FDA approved the first 4-factor Prothrombin Complex Concentrate (PCC), Kcentra, for reversal of warfarin anticoagulation in adults with active bleeding.[2] PCCs are pooled concentrates of human donor plasma containing Factors II, IX, and X (3-factor), with some also containing variable amounts of Factor VII (4-factor).[3] PCCs do not require ABO-typing or thawing so they can be administered quickly.[3] Several studies have shown that PCCs result in a more rapid, effective, and sustained reduction in INR compared to FFP with a lower incidence of adverse reactions.[2-5] PCCs should be considered in addition or as an alternative to FFP in actively bleeding patients who require rapid warfarin reversal.

PCCs should be avoided in patients with a thromboembolic event in the past 3 months,[2] known allergy to the product, DIC, or heparin-induced thrombocytopenia.[3] PCCs are expensive; a single dose of Kcentra (70-kg,INR >6) costs about $4445.[2] This direct cost may be offset by cost savings from more rapid and effective INR reversal and by decreased incidence of adverse reactions compared to FFP, however more cost analysis studies are needed.

References/Suggested Readings:

1. McCullough, J. Transfusion Medicine 3rd Edition. Wiley-Blackwell Publishing. 2012.
2. Kcentra: A 4-Factor Prothrombin complex Concentrate for Reversal of Warfarin Anticoagulation. The Medical Letter on Drugs and Therapeutics. July 2013;1420:53.
3. Cada DJ, Levien TL, Baker DE. Prothrombin Complex Concentrate. Hosp Pharm. Dec 2013; 48 (11): 951-957.
4. Hickey M, Gatien M, Taljaard M, et al. Outcomes of Urgent Warfarin Reversal With Frozen Plasma Versus Prothrombin Complex Concentrate in the Emergency Department. Circulation. June 2013;128:360-364.
5. Dager WE. Developing a Management Plan For Oral Anticoagulant Reversal. American Journal of Health-System Pharmacy. May 2013;70(10):S21-S31.

Send your questions to coberlye@health.missouri.edu to be published in future editions of the Missouri Hospitalist.

Diagnostic Dilemma

Answers:

1) D

ECG shows wide QRS, prominent peaked T waves most likely consistent with findings seen with hyperkalemia. Notice of ECG changes associated with hyperkalemia should be immediately followed by administration of calcium gluconate to stabilize membrane potential.

2) B

The rhythm shown in the ECG is a wide complex tachycardia (WCT). The differentials for WCT are ventricular tachycardia (VT) and supraventricular tachycardia with aberrancy. The most common cause of WCT is VT. There is no evidence of AV dissociation. Applying Brugada morphology criteria, RBBB morphology in V1 with R>r' and qS in lead V6 favors the diagnosis of VT.

3) D

The diagnosis based on ECG is accelerated idioventricular rhythm. This is a benign arrhythmia seen post-reperfusion in acute MI. The arrhythmia is a sign of reperfusion, although not a very good marker in terms of specificity or sensitivity. Observation is sufficient as arrhythmia is self-resolving.

ID Corner

William Salzer, MD
Professor, Division of Infectious Diseases, University of Missouri Health Care

A nice basic review on community acquired pneumonia that addresses some of the controversy on Health Care Associated Pneumonia (HCAP) in Clinical Practice.

Wunderlink RG, GW Waterer. Community-acquired pneumonia. N Engl J Med 2014; 370:543-51.
http://www.nejm.org/doi/pdf/10.1056/NEJMcp1214869

MISSOURI HOSPITALIST SOCIETY

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CONFERENCE CALENDAR

Palliative Care for Hospitalists and Intensivists (PCFHI)
Dates: April 3-5, 2014
Venue: Boston, Massachusetts 02116, United States
http://www.hms.harvard.edu/pallcare/PCFHI/PCFHI.htm

Hospitalist and Emergency Procedures CME Course
Dates: April 5-6, 2014
Venue: San Francisco, California 94111, United States
http://www.hospitalprocedures.org/store/#!/~/product/category=2828269& id=24368249

Comprehensive Stroke Management Update
Dates: April 10-12, 2014
Venue: Hilton Head Island, South Carolina 29928, United States
http://www.hospitalprocedures.org/store/#!/~/product/category=2828269& id=24368249

Care of the Hospitalized Patient 2014
Dates: April 12, 2014
Venue: Saint Louis, Missouri 63110, United States
https://cme.wustl.edu/(S(d0head45rf03yx45zpklio45))/SeminarInfo.aspx?course_code=13114

Hospitalist and Internal Medicine Review and Update: Inpatient and Outpatient Care
Dates: May 12-16, 2014
Venue: Sarasota, Florida 34236, United States
http://www.ams4cme.com/www/LiveSeminars/SEMLA-2820140512.aspx

Ultrasonography for the Hospitalist
Dates: June 18-20, 2014
Venue: Glenview, Illinois 60025, United States
https://cme.wustl.edu/(S(d0head45rf03yx45zpklio45))/SeminarInfo.aspx?course_code=13114

Save the date:

Missouri Chapter of the ACP
September 11-14, 2014
Tan Tar A in Osage Beach, MO
https://www.missouriacp.org/index.php?page_id=69

Note: Three ABIM SEP modules will be presented on Thursday, September 11, 2014 to assist with MOC requirements