**Case Vignette for StuNews:**

**History of Present Illness:** A 67-year-old man presents to the emergency department with nausea, vomiting, and diarrhea. The symptoms have lasted for 2–3 days and have worsened in the past 24 hours. The patient reports no sick contacts, although he knows there is a “nasty stomach bug” going around.

**Medical History:** Chronic systolic heart failure, diabetes mellitus type 2, chronic kidney disease (baseline serum creatinine [SCr] 2.8–3.2 mg/dL [SI 247.5 – 282.9 µmol/L), mechanical mitral valve replacement, benign prostatic hyperplasia

**Social History:** No illicit drugs; quit cigarette smoking 20 years ago; occasional alcohol (1 beer per week); lives with wife, both are retired

**Current Medications:** Carvedilol 25 mg orally twice daily; ramipril 10 mg orally daily; torsemide 40 mg orally daily; spironolactone 25 mg orally daily; insulin glargine 25 units subcutaneously once daily; cholecalciferol 1000 units orally once daily; calcium carbonate 600 mg orally twice daily with meals; warfarin 5 mg orally daily, except for 7.5 mg on Monday and Friday; tamsulosin 0.4 mg orally once daily

**Allergies:** Heparin (thrombocytopenia)

**Vital Signs:** Blood pressure (BP) 98/58 mm Hg; heart rate (HR) 101 beats/minute; respiratory rate (RR) 14 breaths/minute; O2 saturation 96% on room air; pain 4/10; height 68 inches; weight 80 kg

**Laboratory Values:** Sodium 132 mEq/L potassium 2.9 mEq/L; chloride 99 mEq/L; HCO3 28 mEq/L; blood urea nitrogen (BUN) 44 mg/dL; SCr 4.5 mg/dL; glucose 122 mg/dL; calcium 8.1 mg/dL; albumin 3.2 mg/dL; white blood cell count (WBC) 6.2 x 103 cells/mm3; hemoglobin 9.2 mg/dL; hematocrit 32% ; platelet count 240,000/mm3; international normalized ratio (INR) 6.2

**Procedure Data:** None

**Other Data:** You are consulted to manage anticoagulation therapy for this patient after vitamin K 10 mg is administered intravenously in the emergency department. He has no signs of bleeding.

**Question 1**

The patient is prescribed antibiotic therapy for gastroenteritis. Which antibiotic, in combination with warfarin, would have the highest propensity for increasing his INR?

1. Amoxicillin/clavulanate
2. Ceftriaxone
3. Ciprofloxacin
4. Metronidazole

Answer: 4. Metronidazole

Rationale: The correct answer is option 4. Metronidazole interacts at the CYP2C9 isoenzyme, which is metabolized by the most potent isomer of warfarin (S-isomer).

Citation: Ageno W, Gallus AS, Wittkowsky A, et al. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e44S-e88S.

**Question 2**

Regardless of how the prescriber managed the elevated INR in the emergency department, what would your recommendation have been?

1. Hold warfarin and monitor the INR daily.
2. Hold warfarin and recommend vitamin K 10 mg subcutaneously once.
3. Hold warfarin and recommend vitamin K 5 mg intravenously once.
4. Hold warfarin and recommend vitamin K 5 mg orally once.

Answer: 1. Hold warfarin and monitor the INR daily.

Rationale: The correct answer is option 1. Although the INR is elevated, there are no signs of bleeding; therefore, vitamin K is not recommended. The warfarin should be held to allow the INR, which should be monitored daily, to decrease without intervention. Administration of vitamin K could result in a subtherapeutic INR and warfarin resistance for up to 1 week. In some cases, vitamin K is recommended only when the INR is 10 or greater or if there are any signs of minor or major bleeding, regardless of the INR.

Citation: Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e152S-e184S.

**Question 3**

On day 2 of hospitalization, the patient has an INR of 1.8. Your recommendation is:

1. Continue to hold warfarin.
2. Reinitiate warfarin alone.
3. Reinitiate warfarin in addition to enoxaparin.
4. Reinitiate warfarin in addition to intravenous argatroban.

Answer: 4. Reinitiate warfarin in addition to intravenous argatroban.

Rationale: The correct answer is option 4. The patient requires anticoagulation because of his mechanical mitral valve, and as long as his INR is below goal, he is at risk of thromboembolism. Option 2 is incorrect because bridge therapy is needed until the INR is within the therapeutic range because of the patient’s artificial valve. Option 3 is incorrect because of the patient’s history of HIT (heparin-induced thrombocytopenia), which makes enoxaparin contraindicated.

Citations:

1. Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e495S-e530S.

2. Whitlock RP, Sun JC, Fremes SE, et al. Antithrombotic and thrombolytic therapy for valvular heart disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e576S-e600S.

**Question 4**

The patient started warfarin and argatroban on day 2. His INR today (day 3) is 1.8. At what INR level and day of hospitalization could argatroban be discontinued?

1. INR 1.8 (day 3)
2. INR 2.5 (day 4)
3. INR 3.2 (day 5)
4. INR 4.1 (day 6)

Answer: 4. INR 4.1 (day 6)

Rationale: Argatroban should be discontinued when the INR on combined therapy is above 4.0; package labeling recommends overlapping therapy for 4–5 days, making option 4 the best answer. Options 1–3 have a lower INR and shorter duration of therapy overlap than are recommended.

Citations:

1. Ageno W, Gallus AS, Wittkowsky A, et al. Oral anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e44S-e88S.

2. Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(suppl):e152S-e184S.

**Question 5**

The patient has been taking argatroban and warfarin for 1 week. The team wants to discharge the patient home; however, his INR remains subtherapeutic. The physician approaches you about the potential use of fondaparinux as bridge therapy instead of argatroban because fondaparinux therapy can be given as an outpatient. Your assessment is:

1. Agree with the plan, and recommend fondaparinux 7.5 mg subcutaneously once daily until his INR is at goal.
2. Agree with the plan, and recommend fondaparinux 2.5 mg subcutaneously once daily until his INR is at goal.
3. Inform the prescriber that fondaparinux is contraindicated in this patient because of his renal impairment.
4. Inform the prescriber that fondaparinux is contraindicated in this patient because of his heparin allergy.

Answer: 3. Inform the prescriber that fondaparinux is contraindicated in this patient because of his renal impairment.

Rationale: The correct answer is option 3. The patient has an estimated creatinine clearance of less than 30 mL/minute, which would contraindicate fondaparinux use. The patient’s heparin allergy is listed in the package insert as a precaution not a contraindication.

Citations: Arixtra [package insert]. Research Triangle Park, NC: GlaxoSmithKline, 2013.

Papadopoulos S, Flynn JD Lewis DA. Fondaparinux as a Treatment Option for Heparin-Induced Thrombocytopenia. Pharmacotherapy. 2007;27(6):921-926.