ABSTRACT
Here we describe three scenarios in a rehabilitation hospital setting of suddenly elevated International Normalized Ratios (INR) in patients who were placed on anti-coagulation Coumadin therapy prior to rehabilitation. Two stroke patients and one polytrauma patient (motor vehicle accident) with subarachnoid hemorrhage all had normal INR at admission, with no change in diet or medication prior to elevated INR. Within 3-4 days following admission, all three patients exhibited elevated INR that was not responsive to reduced Coumadin. One stroke patient was found to have an abdominal abscess as determined by CT scan at an acute care hospital. The second stroke patient was found to have acute parotiditis. The polytrauma patient was found to have abscess in her left thigh as determined by CT scan at an acute care hospital. These cases suggest that sudden INR elevation may be related to infections secondary to anti-coagulation treatment.

INTRODUCTION
It is well known that INR is very liable in clinical practice. It can be affected by patients’ diet and medications, especially antibiotics, thus management of INR is very challenging. It is very common for patients on Coumadin, for a number of reasons, to be discharged to a rehabilitation unit. As a physician, it is very important to monitor changes in INR, and adjust the dose of Coumadin to avoid sub/supratherapeutic INR. Here we noticed three cases of Coumadin treated patients, initially without a clear reason for elevated INR (diet and changes in medication were ruled out). It was later determined that all three patients were found to have variety of infections, although there was no indication of leukocytosis or temperature prior to elevated INR.

CASE 1
Case 1: A 46 year old female was admitted to our stroke unit due to right middle cerebral artery (MCA) stroke complicated with deep vein thrombosis (DVT). She was on therapeutic Coumadin prior to rehabilitation. Her INR on rehabilitation day 1 through 4 was 1.6, 1.6, 2.6 and 3.4 respectively. Her Coumadin dose was 5 mg until day 2, 2.5 mg on day 3, and held on day 4. Her INR was 3.5 on day 5 (Figure 1). She was admitted to the acute care hospital for fever, and workup with CT indicated an abdominal abscess.

CASE 2
Case 2: A 70 years old female with a right MCA stroke was admitted to the stroke unit, and she was put on therapeutic Coumadin at the acute care hospital due to extension of a prior stroke. On rehabilitation day 1 through 3, her INR was 2.5, 3.0 and 3.1 on 2.5 mg of Coumadin. On day 4, and her INR was 3.3, her Coumadin was held. Repeat INR was 3.3 on day 5 without Coumadin. INR was 1.8 on day 6 and she was given 2 mg of Coumadin. Her INR suddenly increased to 6.9 and 7.2 on day 7 and 8 respectively without Coumadin (Figure 1). On day 6, she complained of right facial pain. Physical examination found tenderness on the right side of her face. Patient was sent to the otolaryngology clinic and diagnosed with acute right parotiditis.

CASE 3
Case 3: A 45 year old female with polytrauma secondary to a motor vehicle accident, was admitted to the brain injury unit due to subarachnoid hemorrhage. She had a history of DVT at the acute care hospital and was placed on therapeutic Coumadin. On rehabilitation day 1 through 3, her INR was 2.1, 2.6, 2.9 on 5 mg of Coumadin. On day 4, her INR was 3.1, her Coumadin was held. Repeat INR was 3.1 on day 5 without Coumadin. INR was 1.9 on day 6 and she was given 2.5 mg of Coumadin. Her INR returned to a therapeutic range on day 7 and 8. On day 9, her INR suddenly elevated to 7.9 (Figure 1). Patient complained of left hip pain, and CT found an abscess in her left lateral thigh.

REFERENCES

DISCUSSION
These cases should alert physicians that an infection should be suspected as a possible etiology if the INR is elevated suddenly to supratherapeutic range without any changes in medication or diet. Coumadin works by inhibiting vitamin K to synthesise clotting factors II, VII, IX, and X [2]. Coumadin is challenging to use due to its narrow therapeutic window, and varying response depending on diet, age, liver function, medications and genetic variations in metabolism [1]. Giardia infection has been reported to increase INR from the therapeutic range [3]. Elevated INR was reported in sepsis patients who did not take Coumadin [4].

FIGURE 1
Figure 1. Time course of sudden elevated INR in three subjects. Case 1 (abdominal abscess): ● with straight line, Case 2 (parotiditis): ○ with dotted line, Case 3 (thigh abscess): ● with dashed line.