REX HEALTHCARE

Laboratory Bulletin...

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Warfarin Reversal Guidelines

The following guidelines for management of warfarin overdose are based upon recent recommendations from the Sixth American College of Chest Physicians Consensus Conference on Antithrombotic Therapy.[1] The 6th ACCP Guidelines were published January 2001. These guidelines recommend using the **oral route** of Vitamin K for warfarin reversal. When this route is not an option, the **IV route** is recommended. An audit of vitamin K use for warfarin reversal at Rex during August 2001 found the oral route was used in 6% of the patients, the IV route in 18%, the intramuscular route in 16%, and 60% of the vitamin K orders were given subcutaneously. The **subcutaneous route** was the recommended route in the 1995 guidelines but this route **has NOT been shown to give consistent and predictable decreases in INR**.[2,3]

Overcorrecting the INR due to overzealous use of vitamin K may occur. If the patient's condition allows conservative management, withholding warfarin is preferable to vitamin K administration. Withholding warfarin minimizes the risk of recurrent thromboembolic disease during the interval between vitamin K therapy and reestablishing adequate warfarin anticoagulation. If clinical circumstances warrant vitamin K use, oral or intravenous administration is preferable to the subcutaneous (sc) route. Due to the risk of anaphylactic reaction during IV administration, the patient must be carefully monitored.

Management of Nontherapeutic INRs

1. For an INR > 3.5 but < 5.0 and no significant bleeding, the warfarin dose should be lowered or omitted. Therapy should be resumed at a lower dose when the INR is at the therapeutic level. If the INR is only minimally above the therapeutic range, no dose reduction may be required.
2. For an INR ≥ 5.0 but < 9.0 and no significant bleeding, omit the next one or two doses. The INR should be monitored daily and warfarin should be resumed at a lower dose when the INR is at the therapeutic level. If it is determined that the patient is at an increased risk of bleeding, omit the next warfarin dose and administer vitamin K, 1.25 to 2.5 mg orally. (Administer vitamin K 2.5 to 5 mg orally if a rapid reversal of warfarin is necessary for urgent surgery. An additional 1.25 to 2.5 mg orally may be given if needed).
3. For an INR ≥ 9.0 and no significant bleeding, warfarin should be held and vitamin K, 3.75 to 5 mg administered orally, with the expectation that the INR will be reduced substantially in 24 to 48 hr. The INR should be monitored daily and additional vitamin K administered if needed. Resume warfarin therapy at a lower dose when the INR reaches the therapeutic level.
4. For life threatening bleeding or unstable patients requiring immediate surgery, give vitamin K 10mg by IV infusion over 20 min. supplemented with FFP (10 ml/kg or 2-3 units for an adult). Monitor patient for anaphylactic reaction during infusion as per vitamin K administration policy. Monitor PT q 6 hr. Repeat vitamin K administration every 12 hours or as needed.

* If the patient is NPO or for some other reason the oral route is not an effective

route, administer vitamin K at the indicated dose via IV infusion.

Management of Oral Anticoagulation During Invasive Procedures

1. For low-risk patients (e.g. patients who have been without venous thromboembolism for > 3 months or patients who have experienced atrial fibrillation without history of a stroke), warfarin therapy should be stopped 4 days prior to surgery. Allow the INR to return to a near-normal level. An INR of 1.5 provides sufficient hemostasis for surgical procedures. If the intervention itself creates a higher risk of thrombosis, administer postoperative low-dose heparin 5,000 units sc every 12 hours or prophylactic low-molecular weight heparin (LMWH) [e.g. enoxaparin 40 mg sc qd or, for post-surgical orthopedic patients, 30 mg sc every 12 hours] and simultaneously begin warfarin therapy.
2. For patients with an intermediate-risk of developing a thromboembolism, stop warfarin therapy approximately 4 days before surgery. Allow the INR to decrease (≤ 1.5). Two days prior to surgery begin low-dose heparin, 5,000 units sc every 12 hours, or LMWH (e.g. enoxaparin 40 mg qd, or for post-surgical orthopedic patients, 30 mg every 12 hours). Continue low-dose heparin or (low-molecular weight heparin) after surgery and begin warfarin.
3. For patients with high risk of thromboembolism (e.g. patients with a history of a thromboembolism within the last 3 months, or patients with a mechanical cardiac valve in the mitral position or an old model of cardiac valve [ball/cage]), stop warfarin therapy 4 days prior to surgery. Allow the INR to decrease (≤ 1.5) and begin therapy 2 days before surgery with full-dose heparin or full-dose LMWH. Heparin can be administered by the following methods:
    - SC injection on an outpatient basis.
    - Continuous IV infusion after hospital admission in preparation for surgery. It can be discontinued 5 hr before surgery with the expectation that the anticoagulant effect will have worn off at the time of surgery.
    - Continue administration of sc heparin or LMWH, stopping therapy 12 to 24h before surgery.

Pharmacy Assistance with Anticoagulation

The Rex Pharmacy offers assistance to physicians with patients requiring reversal of anticoagulation. There is a **Rex Pharmacy Warfarin Reversal Protocol** for patients who have a non-therapeutic INR and **do not have significant bleeding**. A physician must write an order for warfarin reversal protocol or pharmacy to dose vitamin K. A pharmacist will monitor the PT/INR daily and make appropriate suggestions until the physician resumes warfarin, the patient goes to surgery, or warfarin is discontinued indefinitely. The **physician must state if a patient will require surgery within 24 to 48 hours. The physician must restart and then manage warfarin therapy.**

In addition, there is a new Lovenox Order Set. The physician must order **"Lovenox per order set FOR _____"** (must state one of the following indications: unstable angina, non-Q-wave MI, acute DVT or prophylaxis). The nurse may complete the order set. Lovenox is **NOT** recommended in patients with a serum creatinine > 2.0 mg/dL or in patients who weigh > 150 kg. The order set will ensure that the patient receives all recommended labs, the correct dose of Lovenox, appropriate initiation of warfarin, and education for DVT patients and families prior to discharge. The physician should adjust warfarin based on the INR by day 3 and thereafter. When appropriate, the physician must order Lovenox to be discontinued (there is no automatic stop time).

For questions or concerns about the Pharmacy anticoagulation service, call **784-3015** and ask to speak to a pharmacist.

Dawn Guy, RPh
John Benson, MD

1. Hirsh J, Dalen J, Guyatt G, *et al*. Managing Oral Anticoagulant Therapy. *Chest* 119(1): 22S-38S, 2001.
2. Benson JD, Leibowitz SM, Morris T. Guidelines for Warfarin (Coumadin) Reversal. *Rex Laboratory Bulletin* 16, January 1997
3. Hirsh J *et al*. Oral Anticoagulants: Mechanism of Action, Clinical Effectiveness, and Optimal Therapeutic Range. *Chest* 108:231S-246S, 1995.

The authors are indebted to the following individuals for assistance in developing the Rex Pharmacy Warfarin Reversal Protocol: Cherine Ali RPh, Robert Bruner MD, Martha Johnson PharmD, Wayne Smith MD, Sean Tehrani MD, and Ken Zeitler MD.

As Flu Season Approaches...

A previous article in the Laboratory Bulletin discussed the new influenza A and B antigen test introduced in the 4th quarter of 2000. Respiratory syncytial virus (RSV) antigen testing has been available since 1989. A look-back at last year's flu season may be of some interest to physicians considering the use of these tests. Last year, a total of 70 influenza tests were ordered, most in January and February of 2001. Of these, 26 (37%) were positive. In a similar 12-month period, 60 of 166 RSV antigen tests (36%) were positive.

Since both of the tests for viral organisms are antigen based, viable organisms are not required. However, the method of specimen collection is very important for the sensitivity of both tests. Using a nasopharyngeal swab maximizes the influenza optical immunoassay test, while a nasopharyngeal aspirate is preferred for the RSV test. The RSV antigen nasopharyngeal aspiration kits and nasopharyngeal swabs for influenza specimens are available from the Client Service representative (784-3355). We recommend collecting specimens in the office, since it eliminates an additional trip to the laboratory.* Test turnaround time is 1- 2 hours after receipt in the laboratory and both tests are offered during first and second shift hours.

John P. Sorge, MD

* Historically, the Rex pathologists have collected nasopharyngeal specimens on patients referred to the Laboratory for RSV or Bordetella pertussis testing. We are pleased to announce that the Rex Respiratory Therapy staff has agreed to assist in collecting these specimens. The author is indebted to Sheila Smithey and Duwayne Engman for assistance in collecting the "look back" data.

Change in Anticoagulant Concentration

On December 3, 2001 the normal range values for the PT (prothrombin time), APTT (activated partial thromboplastin time), TCT (thrombin clotting time) and fibrinogen will change to reflect the lower citrate anticoagulant concentration used in the specimen tubes. The decrease in concentration of sodium citrate from 3.8% to 3.2% results in less bound calcium. This change is recommended by the International Society of Thrombosis and Hemostasis (ISTH) and the National Committee on Clinical Laboratory Standards (NCCLS) because it will decrease variability in the

clotting times related to the variance in hematocrit and filling volumes of the tubes. The change results in slightly shorter times. Outpatient specimens for prothrombin times received in tubes containing 3.8% citrate will be reported in seconds without the international normalized ratio (INR) value and a comment explaining the reason for not reporting the INR. The results of the study of 426 specimens run at Rex Lab for comparison is listed below. Note the fibrinogen method has been changed to reflect a national trend.

NORMAL RANGE STUDY USING 3.2% vs. 3.8% SODIUM CITRATE

TEST RANGE	**NORMAL RANGE (3.2% sodium citrate)**	**NORMAL (3.8% sodium citrate)**
PT	**11.3-13.7**	**11.8-13.8**
PTT	**22.7-36.5**	**24.0-35.0**
TCT	**12.9-18.1**	**15.0-20.0**
Fibrinogen	**178.0-504.9** (mechanical)	**150-418** (photo optical)

Stephen Chiavetta, MD
Elaine Patterson, MT

Reference Test Results "On Line"

Effective December 4, 2001, test results on most types of specimens referred to Mayo Medical Laboratories for evaluation will be available for review using the Clinical Workstation program on the Rex Healthcare intranet. The results will also be incorporated into the Rex Laboratory cumulative report, eliminating the current separate page format. Results for interpretive reports (e.g. surgical pathology consults) will not be available by this format. Members of the laboratory staff, Information Technology Department, and Mayo Medical Laboratories constructed the interface between Mayo and Rex in a collaborative effort. We hope this enhancement will assist patient care by improving report turnaround time and accessibility of test results.

Deborah Brown, MT

For further information, call the Laboratory (784-3040). Telephone extensions are: Pathologists' Direct Line (3201), Sharon Logue (Lab Director 2400), Robin Ivosic (Core Lab Manager 3053), Elaine Patterson (Core Lab Manager 3054), Jackie Okoth (Core Lab PM Manager 4248), Diane Young (Anatomic Pathology Manager 3888), Nga Moore (Customer Service Manager 3396), Kori Horsley (Customer Service PM Manager 4340).