

## 27. INRs that fluctuate

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**Q: "I have been taking 15 mg coumadin® a day for nearly a year and my INR was staying relatively o.k. 'till about 2 weeks ago, when it was found to be 1.0. My coumadin was increased to 17.5 mg a day and Lovenox® shots added. My next INR had dropped to 0.8. What could be causing this sudden problem?"**

A: Whenever an INR value is significantly higher or lower than usual in a patient whose INRs have been relatively stable and well controlled, the following reasons should be considered by patient and physician:

1. Lab error: Was the out-of-line INR a lab error (significant trouble at the time of blood draw with tissue trauma before blood could be obtained; the blood tube was not filled appropriately)? It may be indicated to repeat the test to confirm that the INR is out of line.
2. New prescription medication: Has any new prescription medication been started or has any old medication been discontinued?
3. Over-the-counter medications: Is the patient taking any new types of over-the-counter medications, vitamins, herbs, homoeopathic medications, weight control pills?
4. Time of medication intake: Is the patient taking his/her various medications at the same times as always or are any medications taken closer to the time when the coumadin is taken? Some drugs interfere with the absorption of coumadin and should therefore not be taken at the same time.
5. Diet: Have there been dietary changes that would change the patient's vitamin K intake? In my opinion, a patient should be familiar with the approximate vitamin K content of the foods that he/she eats.
6. Infection: Has the patient recently had an infection or diarrhea? Both can increase the INR.
7. Compliance: Has the patient really taken his/her medication or has he/she taken too much warfarin? Since various generic warfarin preparations and coumadin all look different, the switch from one drug to the other can lead to incorrect medication intake.
8. Lupus anticoagulant: Does the patient have a lupus anticoagulant? In some patients the lupus anticoagulant can have an influence on the INR. Since lupus anticoagulant levels can fluctuate over time, the INR can fluctuate as well. Furthermore, if the lab changes its reagents or the INR is tested in different labs, discrepant INR results are possible in some patients with lupus anticoagulants.
9. Shelf life: Was the coumadin outdated? Efficacy of the drug is only guaranteed for the time printed on the package. The drug may lose efficacy thereafter.
10. Stress, physical activity: Has there been an unusual amount of stress, sleep deprivation, or physical activity in the days preceding the INR test? While I am not aware of any published data on this issue, it is possible that in some patients there may be an influence on the INR (increase or decrease), possibly through an influence on the metabolism of coumadin.
11. Generic warfarin: Could (a) taking generic warfarin, or (b) switching from brand coumadin to generic warfarin or vice versa, or (c) switching from one type of generic warfarin to another generic warfarin explain INR fluctuations? Unlikely. Studies indicate that generic warfarin and brand coumadin are equally effective and bioequivalent, i.e. for example 5 mg coumadin leads to the same INR as 5 mg generic warfarin [reference 1]. However, an individual patient assessment is needed, with correlation of INR values to the time of use of generic warfarin or brand coumadin, to help clarify whether the fact that a patient is taking generic warfarin may play a role in the INR fluctuations.