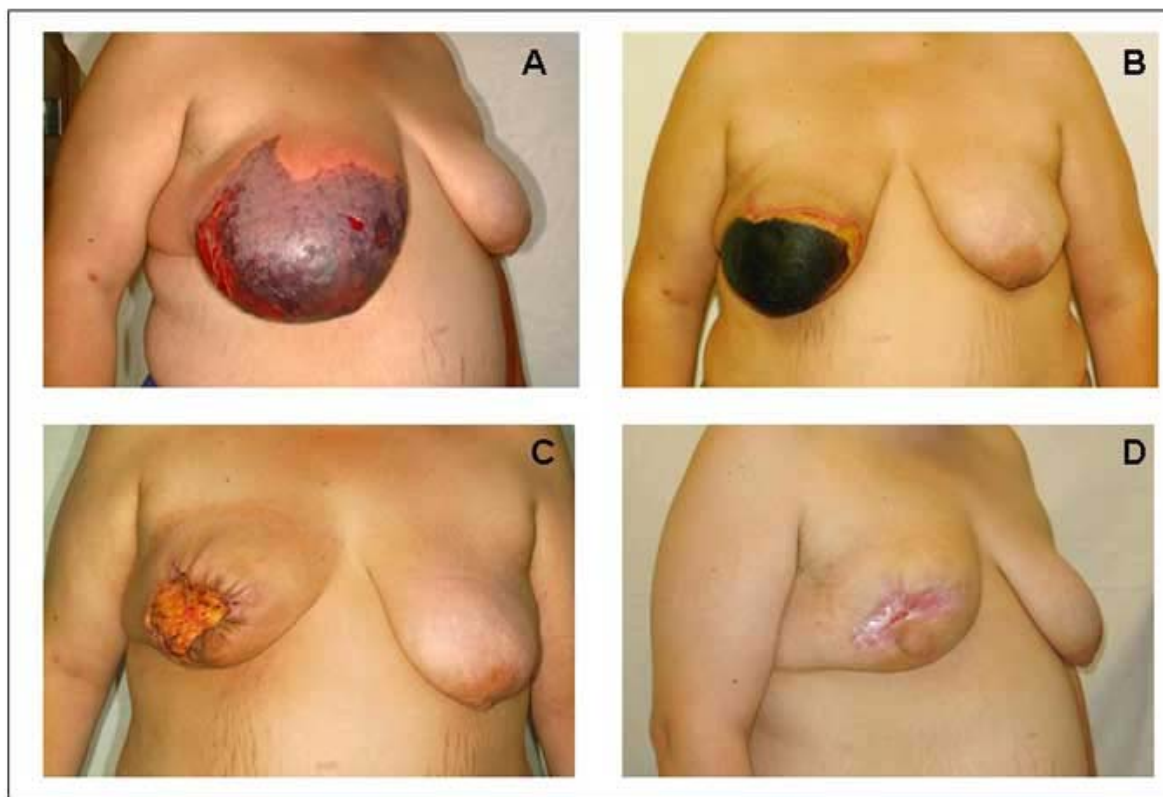


## 86. Warfarin induced skin necrosis

*Last Updated: 9/9/2005*

### Case Report:

A young woman with an acute pulmonary embolism (PE) is admitted to the hospital and started on intravenous heparin. Warfarin (Coumadin®) at a dose of 10 mg per day is also started. Very quickly, within 2 days, the INR is 3.5 and heparin is stopped. On day 5, the patient develops severe pain, purple discoloration, and swelling in her right breast (Figure A). Warfarin-induced skin necrosis is diagnosed. Warfarin is stopped, heparin restarted. Very powerful intravenous pain medication (narcotics) only partially controls the patient's pain. The discoloration and swelling worsen over the next several days. Finally, after about 10 days, her pain becomes somewhat bearable. She is discharged home after a 15 day hospital stay on low molecular weight heparin (Lovenox®) and oral pain medication. Four weeks after the beginning of symptoms, the dead tissue of her breast has turned black (Figure B). Two months later the dead tissue of the breast is surgically removed (Figure C). After 6 months, the breast is almost completely healed (Figure C). Clotting work-up shows that the patient has heterozygous factor V Leiden. Protein C and S levels and other thrombophilia tests are normal. (Case has been published in the medical literature, reference 3).



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### Discussion:

Warfarin-induced skin necrosis is a rare complication of warfarin (coumadin®) therapy. It only occurs in approximately 1 of 10,000 patients treated with warfarin. It occurs within the first few days of warfarin therapy. People at particular risk are those (a) who receive high initial doses of warfarin, and (b) in whom heparin therapy is given for shorter than 5 days (such as in this patient). Patients with underlying clotting disorder, such as protein C or S deficiency, may be at particular risk. However, Warfarin-induced skin necrosis has also developed in patients who have no identifiable clotting disorders (thrombophilia). The disorder occurs more commonly in women and in individuals who are overweight.

"Necrosis" means "dead tissue". Patients with Warfarin-induced skin necrosis develop very painful skin areas, most

commonly in the breasts, followed by buttocks, thighs and abdomen. Warfarin-induced skin necrosis happens because blood clots form in the blood vessels of the skin and the underlying fat tissue. The clots prevent blood flowing to the skin and fat tissue, leading to insufficient oxygen delivery. Skin and fat tissue therefore die. Bleeding into the dead tissue then occurs, leading to the bluish-purple discoloration. This leads to the swelling. The swelling and the lack of oxygen cause the extreme pain. Later, the dead tissue turns black - this is referred to as gangrene. Often, the dead tissue eventually has to be removed surgically. Finally, the skin will heal.

The reason why Warfarin-induced skin necrosis occurs in some patients and not in others is not completely clear. Biopsies of the involved areas show that there are clots in the blood vessels of the skin and fat tissue. This is a paradoxical reaction, which is well known: in the first few days of warfarin therapy blood actually clots more easily (becomes "thicker"), before it eventually (after approximately 5 days) "thins" the blood. To protect patients from this paradoxical initial blood "thickening" effect of warfarin, the blood thinners heparin or low molecular weight heparins (Fragmin®, Lovenox®, or Innohep®) are often given for the first few (at least 5 days) of warfarin therapy.

Theories exist why these blood clots happen on warfarin. The following explanation is meant for the scientifically interested reader: Lowering of the natural anticoagulant protein C (half-life: 9 hours) leads to a hypercoagulable state in the first few days of warfarin initiation, before lowering of prothrombin (half-life: 60 hours) leads to protective anticoagulation.

#### References:

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