had similar and dramatic reductions of the number of anginal attacks (91% and 86%, respectively), episodes of silent ischemia (56% and 46%, respectively), and duration of ischemia (66% and 61%, respectively). Aspirin therapy did not significantly affect any of the major outcomes. The only bleeding complications recorded were minor, with 2 patients each in the aspirin and IV heparin groups reporting epistaxis or ecchymosis.

Recommendations for clinical practice. **This study provides strong evidence of the superiority of heparin for short-term relief of persistent chest pain and silent ischemia in patients with unstable angina. The evidence is relatively strong that subcutaneous heparin works as well as intravenous heparin, although we await a study that has the power to make a definitive comparison between the two regimens. Given the ease, low cost, and possibility of outpatient use, it would be reasonable to give subcutaneous heparin to patients who are stable but have persistent chest pain. A larger study addressing patient-oriented outcomes, such as reinfarction rates and long-term efficacy and survival, is needed.**

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VENOUS THROMBOEMBOLISM

TITLE: A Comparison of six weeks with six months of oral anticoagulant therapy after a first episode of venous thromboembolism
AUTHORS: Schulman S, Rhedlin A
JOURNAL: *The New England Journal of Medicine*
DATE: June 22, 1995; Volume 332:1661–5

Clinical question. **Following an initial episode of deep-venous thrombosis (DVT) or pulmonary embolism (PE), what is the comparative efficacy of 6 weeks vs 6 months of oral anticoagulant therapy in preventing recurrence of venous thromboembolism?**

Background. Although secondary prophylaxis with oral coagulation is routinely given for deep-venous thrombosis and pulmonary embolism, the optimal duration of therapy is open to debate. Several randomized trials have suggested that the duration of anticoagulation can be shortened from a few months to a few weeks without increasing the risk of recurrence. Some of these studies, however, have been criticized for either an inadequate sample size or a lack of objective criteria for the diagnosis of venous thromboembolism.

Population studied. Patients studied included individuals at least 15 years old who presented to one of 16 medical centers in Sweden with an acute pulmonary embolism or deep-vein thrombosis in the leg, iliac veins, or both. Initial diagnoses were confirmed by venography in cases of deep-vein thrombosis and with perfusion-ventilation scanning or angiography in cases of pulmonary embolism.

Of 1185 patients evaluated at the 12 hospitals that kept logs of encounters, 40% were excluded on the basis of the following prespecified criteria: absence of radiographically confirmed venous thromboembolus, pregnancy, allergy to study medications, an indication for continuous oral anticoagulation, total paresis, venous ulcer or arterial insufficiency of the affected leg, congenital deficiency of antithrombin III, protein S or protein C, unwillingness to give oral consent, and unavailability for follow-up. The proportion of patients excluded for any particular reason was not specified. It would have been useful to know whether patients were excluded largely on the basis of medical contraindications or refusal to participate since these reasons for exclusion would result in different samples of patients and have very different implications for the generalizability (also called external validity) of the study.

Study design and validity. This study was a randomized controlled trial. After at least 5 days of intravenous or subcutaneous heparin, 897 patients were randomly assigned to either 6 weeks (n=443) or 6 months (n=454) of oral anticoagulation. Patients received warfarin or dicoumarin with a targeted international normalized ratio (INR) of 2.0 to 2.5, and were followed for 2 years. Comparison of the two treatment groups revealed similarities across a number of characteristics including sex, family history, and site of and risk factors for thromboembolism. The treatment groups differed in that fewer patients in the 6-week group had previously received thrombolytic therapy. However, the total number of patients who had such therapy was small, and thus not likely to make a difference. A few patients in both treatment groups also received oral anticoagulation for either a longer or shorter period than intended. The mean duration of treatment, however, increased by less than 0.1 month per patient and probably would have an insignificant impact on the results.

Outcomes measured. The principal endpoints of the trial were major hemorrhage during oral anticoagulation, recurrent venous thromboembolism, and death during a 2-year study period.

Results. The authors found a significant difference in the incidence of recurrent thromboembolism between groups treated with oral anticoagulation for 6 weeks (18%) and those treated for 6 months (9.5%). In the 6-week group, discontinuation of treatment was associated with an immediate increase in the rate of recurrence that stabilized at 6 months. Analysis of patients grouped by predisposing risk factors, such as family history or size of venous thromboembolism and effectiveness of oral anticoagulation, consistently revealed a 50% reduction in the risk of recurrence when treatment was given for 6 months instead of 6 weeks. However, after 6 months, both treatment groups continued to experience a linear increase in the cumulative risk of recurrence corresponding to 5% to 6% annually. One patient in the 6-week group and five in the 6-month group experienced a major nonfatal hemorrhage but the difference was not statistically significant. There was no significant difference in mortality between the two treatment groups.

Recommendations for clinical practice. **The study found that after an episode of DVT or PE, there was a 50% reduction in recurrent thromboembolism for 6 weeks compared with 6 months of oral anticoagulant therapy. These findings suggest three important points to consider when prescribing warfarin therapy: 6 weeks of oral anticoagulant therapy is inadequate; longer courses of therapy are not associated with an increase in bleeding complications; and regardless of treatment length, patients will continue to experience a definite risk of long-term recurrence and, therefore, should be aware of the signs and symptoms of recurrent disease.**

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BACTERIAL VAGINOSIS

TITLE: Treatment of bacterial vaginosis: a comparison of oral metronidazole, metronidazole vaginal gel, and clindamycin vaginal cream
AUTHORS: Ferris DG, Litaker MS, Woodward L, Mathis D, Hendrich J
JOURNAL: *The Journal of Family Practice*
DATE: November 1995; 41:443–49

Clinical question. **What is the comparative efficacy of oral metronidazole, metronidazole vaginal gel, and clindamycin vaginal cream for the treatment of bacterial vaginosis?**

Background. Bacterial vaginosis accounts for approximately one half of all cases of symptomatic vaginal infections diagnosed in an outpatient practice. It is associated with an increased risk for pelvic and posthysterectomy infections, as well as serious adverse obstetrical outcomes including premature rupture of membranes, preterm labor, and postcesarean endometritis. Oral metronidazole, the most commonly used treatment, is highly effective. However, concerns about the systemic side effects and potential but unproven teratogenicity in early pregnancy have prompted the search for alternative therapies. Intravaginal metronidazole and clindamycin, both of which reduce systemic absorption and treat the infection at its source, are potentially effective and provide a safer means of treating bacterial vaginosis in both pregnant and nonpregnant women.

Population studied. The original study population included 101 clinic patients who were 15 years or older and had symptoms and laboratory evidence of a vaginal infection positive for clue cells, "sniff" test, or DNA probe test. At the conclusion of the study, data were available for only 72 of the participants. Of the unevaluable participants, the largest proportion, 12, were excluded for failure to return for the follow-up appointment. However, the three treatment groups did not differ with respect to the number of patients who failed to follow up.

Study design and validity. The study was a randomized trial of the efficacy of treatment for bacterial vaginosis with either oral metronidazole 500 mg twice a day for 7 days, metronidazole vaginal gel 5 g twice a day for 5 days, or clindamycin vaginal cream 5 g once a day for 7 days. The choice of this study design is commendable since randomized trials are the optimal method to compare different treatments. The potential for systematic error or bias might have been further reduced with the use of placebo control and blinding. Another positive feature of the study was the use of several methods, including a newer DNA probe for *Gardnerella vaginalis*, rather than only one method to identify bacterial vaginosis. This study nicely illustrates that therapeutic response can vary according to the diagnostic criteria used.

Evaluation of short-term cure rates only is one limitation of this study. Because bacterial vaginosis is often recurrent, short-term cure rates can be overly optimistic and misleading. A second limitation of this study is the small sample size. With only a few patients in each treatment group, the probability of saying that there is no difference among treatments when one actually exists is .60. Ideally, this value (known as beta) should be less than .20. Another way of looking at this is to consider the power of the study. Power refers to the probability that a trial will find a statistically significant difference when such