CLINICAL CONSULTATION

Answers to readers' questions on:

- *Therapy for deep venous thrombosis*
- *Therapy for RSV bronchiolitis in infants*

Therapy for DVT: The importance of the thrombus site

What is the significance of the location of deep venous thrombosis (DVT), with respect to treatment and the risk of recurrence?

In patients with lower-limb DVT, the cause is a major determinant of recurrent disease: patients with idiopathic (unprovoked) DVT have a 4- to 6-fold greater risk of recurrent disease compared with patients with secondary DVT, which occurs after exposure to a transient risk factor (such as surgery).

However, there is emerging evidence that the location of DVT also is an important determinant of recurrence and should be considered in making decisions about both the aggressiveness of the initial antithrombotic therapy and the duration of oral anticoagulation therapy (Table). Patients with DVT can be classified into 3 prognostic groups, based on the location of DVT:

- Distal (calf) DVT.
- Submassive proximal DVT that involves the popliteal or femoral vein.
- Massive iliofemoral DVT that involves the iliac vein and possibly the inferior vena cava.

In patients with distal DVT that is limited to the calf veins, the prognosis is good, with a recurrence rate of 1% to 3% per year after diagnosis. However, until recently, the optimal duration of anticoagulation therapy was unclear, particularly in patients with idiopathic calf DVT. A recent clinical trial involving such patients found that 6 weeks was as effective as 3 months of therapy in preventing recurrence (2.6% vs 2%, respectively).[1] Thus, in patients with idiopathic or secondary calf DVT, 6 weeks of anticoagulation therapy is sufficient.

More than 80% of patients with DVT have submassive proximal DVT. The initial treatment for this group involves 4 to 6 days of intravenous unfractionated heparin, with a target partial thromboplastin time 1.5 to 2 times the control value, or weight-adjusted fixed-dose low molecular weight heparin, administered once or twice daily by subcutaneous injection. An oral anticoagulant such as warfarin usually is initiated on the first day of heparin therapy and is administered to achieve a targeted international normalized ratio of 2.0 to 3.0.

More aggressive antithrombotic therapy is not required in such patients unless there is evidence of venous limb ischemia, which is unusual in patients with DVT that is limited to the popliteal or femoral vein. After the initial 4 to 6 days of therapy with a heparin preparation, at least 6 months of oral anticoagulation therapy is recommended for patients with idiopathic DVT, while 3 months is sufficient for those with secondary DVT.[1,2] In patients with an ongoing risk factor, such as cancer or a hypercoagulable blood abnormality, long-term anticoagulation therapy is recommended.

In patients with massive iliofemoral DVT, it traditionally was assumed that unless they had limb-threatening venous ischemia, they should be treated the same way as patients with less extensive popliteal or femoral DVT. However, a recent study found that conventional initial antithrombotic therapy, consisting of 4 to 6 days of a heparin preparation, was inadequate in patients with iliofemoral DVT.[3]

In this study, which excluded patients with venous limb ischemia, patients with iliofemoral DVT had a

Table – Recommended therapy for patients with DVT

DVT type and location	Suggested initial antithrombotic therapy	Duration of oral anticoagulant therapy
Distal DVT (calf veins only)	4 - 6 days of UFH or LMWH	6 weeks
Submassive proximal DVT (popliteal or femoral vein)	4 - 6 days of UFH or LMWH	• Secondary DVT: 3 months • Idiopathic DVT: ≥ 6 months • Patients with ongoing risk factor: indefinite
Massive iliofemoral DVT (iliac vein ± IVC)	10 - 14 days of UFH or LMWH Thrombolytic therapy	≥ 6 months

DVT, deep venous thrombosis; UFH, unfractionated heparin; LMWH, low molecular weight heparin; IVC, inferior vena cava.

greater than 2-fold higher risk of recurrent disease than those with popliteal or femoral DVT if they received conventional antithrombotic therapy (11.8% vs 5.2%, respectively; odds ratio, 2.4). Results suggest that patients with iliofemoral DVT should receive more aggressive initial antithrombotic therapy, consisting of 10 to 14 days of a heparin preparation or thrombolytic therapy.

Thus, the location of DVT is an important consideration when deciding the aggressiveness of initial antithrombotic therapy and the duration of oral anticoagulant therapy.

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2. Hyers TM, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease. *Chest.* 2001;119:176S-193S.

3. Douketis JD, Foster GA, Crowther MA, Ginsberg JS. Does the location of thrombosis determine the risk of disease recurrence in patients with proximal deep vein thrombosis? *Am J Med.* 2001;110:515-519.

RSV bronchiolitis: A close look at treatment efficacy

How effective is ribavirin for the treatment of respiratory syncytial virus (RSV) bronchiolitis in infants? What other interventions do you recommend for reducing airway reactivity following bronchiolitis?

■ Ribavirin was first reported to be effective in RSV bronchiolitis in the mid-1980s. A few small trials indicated improved oxygenation in recipients of ribavirin aerosol compared with those who received a distilled-water placebo. In one study of persons receiving mechanically assisted ventilation, ribavirin appeared to reduce the amount of time on ventilatory assistance and the duration of stays in the ICU.[1]

These results were challenged on numerous fronts, especially concerning the use of water as a placebo, since inhalation of water can induce bronchospasm in persons with inflamed airways. The high cost of ribavirin, the requirement for a special nebulizer, and a concern (probably misplaced) about teratogenicity of the drug in humans have further restricted its use in most centers.

A recent meta-analysis concluded that in virtually all appropriately designed, controlled, double-blind studies of ribavirin, a minor benefit was found following use of the drug, with an overall tendency toward reduced mortality.[2] However, because supportive care for infants in respiratory failure continues to improve, deaths from RSV infection are now quite uncommon, even in infants with underlying heart and lung disease. Currently, ribavirin is almost never used at our hospital.

With regard to airway reactivity following bronchiolitis, it is well known that infants with bronchiolitis (particularly that caused by RSV) have recurrent episodes of wheezing in early childhood and during school-age years. Therefore, many physicians have asked whether RSV infection in infancy induces persistent airway hyperreactivity and whether intervention at the time of RSV infection might reduce this airway hyperresponsiveness.

It is not certain that RSV infection induces persistent airway hyperreactivity or the recurrent wheezing observed in infants following bronchiolitis. Wheezing with RSV infection may simply serve as a marker for some underlying tendency of the airway to become obstructed during viral infections in infancy and with allergen exposure in later life.

Indeed, most studies of corticosteroids or cromolyn (or ribavirin) administered during RSV bronchiolitis in infancy have failed to demonstrate any positive effect on the incidence of subsequent wheezing. Studies on the effect of antileukotriene therapy following bronchiolitis are under way, but the results are not yet available.

In summary, we manage essentially all cases of RSV bronchiolitis with only fluid and oxygen supplementation, without antiviral, bronchodilator, or anti-inflammatory therapy.

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2. Randolph AG, Wang EEL. Ribavirin for respiratory syncytial virus lower respiratory tract infection. *Arch Pediatr Adolesc Med.* 1996;150:942-947.

We welcome brief questions on general clinical problems related to respiratory medicine, including brief descriptions of confusing patient situations or follow-up questions on articles we have published. The most interesting and broadly applicable queries and replies will be published. (Names will be withheld on request.) Address correspondence to the Editor, *The Journal of Respiratory Diseases*, 330 Boston Post Road, PO Box 4027, Darien, CT 06820-4027. You can also e-mail us via sarah.williams@scp.com.