



Messing with Mother Nature

Even the most effective, cleverly targeted therapies may come with unintended consequences. Heparin can prevent clots, but may decrease platelets and cause thrombosis. Antibiotics miraculously vanquish infection, but their repeated use sows the seeds of resistance.

The challenge for clinicians is to find where the benefits of a therapy outweigh the risks, and when untoward effects occur, how to manage them.

On page 341 of this month's issue of the *Journal*, Dr. Joseph Broderick discusses the novel use of a coagulation factor (recombinant factor VIIa) as a treatment for hemorrhagic stroke. In a multicenter trial that was a tour de force in getting patients recruited and treated early,¹ this drug limited stroke extension and improved functional outcomes and survival.

However, as we recently learned from the use of selective COX-2 drugs,² messing with Mother Nature's finely tuned hemostatic homeostasis may not be without cost: do we need to be concerned about any increase in nonfatal myocardial infarctions with the use of this drug in this setting? The number of events was too small to permit any conclusion, and this concern may not be realized in larger studies or may not counterbalance the exciting benefits of this unique approach. In addition, this drug might be useful in other settings of difficult-to-control hemorrhage. Perhaps in the future we can be clever enough to formulate medications to target specific vascular beds, avoiding unwanted thrombosis.

We have witnessed the gratifying, if limited, success of highly active antiretroviral therapy in patients with human immunodeficiency virus (HIV) infection. On page 285, Drs. Alan Taege and Wendy Armstrong discuss the possible emergence of a highly resistant and highly virulent strain of HIV. Whether this is aberrancy or an unwelcome trend remains to be seen. As Jeff Goldblum's character said in the movie *Jurassic Park*, "life finds a way": no matter how clever we are with our biologic and molecular targeting of antiretroviral therapies, the virus seems to have ways to keep eluding our strategies.

As our technologic and intellectual advances roll forward, we need to keep things in perspective. Drs. Taege and Armstrong end by calling for a redoubling of our public health efforts to prevent HIV infections in the first place. Amen to that.

BRIAN F. MANDELL, MD, PhD
Editor-in-Chief

REFERENCES

1. Mayer SA, Brun NC, Begtrup K, et al, for the Recombinant Activated Factor VII Intracerebral Hemorrhage Trial Investigators. Recombinant activated factor VII for acute intracerebral hemorrhage. *N Engl J Med* 2005; 352:777-785.
2. Karha J, Topol EJ. The sad story of Vioxx, and what we should learn from it. *Cleve Clin J Med* 2004; 71:933-939.