



Research Update • Le point sur la recherche

New window on inhibiting clotting

An Alberta researcher has found a new and powerful technique to prevent the formation of blood clots. The finding opens a window on new possibilities in the prevention of inappropriate clotting.

Dr. Marek Radomski, a professor of pharmacology at the University of Alberta, has found that inhibiting a protein called gelatinase A prevents aggregation of platelet cells to a degree that far surpasses the effects of current anticlotting treatments. The research was recently published in *Nature* (1997;386:616).

Radomski's team manipulated healthy blood samples in different ways to prevent clotting. Initial tests used ASA, which blocks production of a clot-promoting substance called thromboxane A₂. Efforts were then increased with the introduction of an antagonist of the enzyme ADP to prevent aggregation. During the final phase, researchers introduced an inhibitor of the protein gelatinase A to healthy blood.

Until the gelatinase A inhibitor was introduced, the best results showed that 40% to 50% of clotting could not be inhibited. Then Radomski's team discovered that inhibiting the action of gelatinase A had a profound effect on platelet aggregation.

"We were able to completely inhibit this action with gelatinase," Radomski said. "We seemed to have discovered a way that is more efficacious than Aspirin to inhibit aggregation. Under the circumstances when As-

pirin is not effective enough, inhibitors of gelatinase A are more effective."

Radomski hopes that his research can help prevent inappropriate formation of clots. The mechanism could help treat patients suffering from vascular disorders that compromise vessel walls and recruit clot-forming cells for the wrong reasons.

"We have opened a window and through this window we can see something that is very promising."
— R. Cairney

Steroids get in your eyes

People with asthma who regularly take high doses of inhaled steroids are at a higher-than-normal risk for glaucoma, reveals a study by Montreal researchers Edeltraut Garbe, Jacques LeLorier, Jean-François Boivin and Samy Suissa, published in the *Journal of the American Medical Association* (1997;277:722-7). But, the researchers stress, that does not mean that people with asthma should stop taking inhaled steroids.

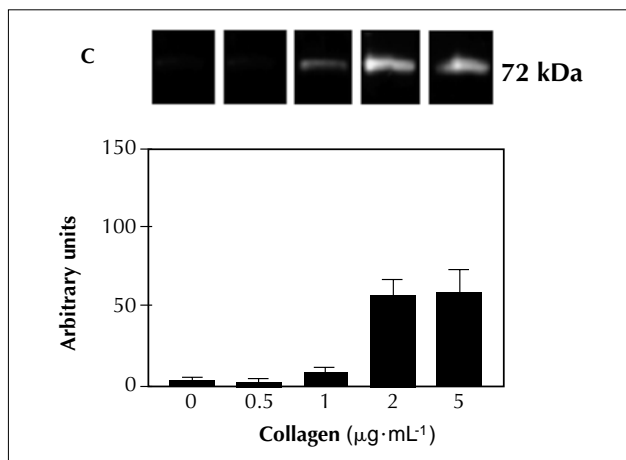
"We've known all along that topical corticosteroids increase ocular pressure," explains Suissa. "And we noted that guidelines for asthma treatment are suggesting higher and higher doses of inhaled corticosteroids." The researchers speculated that inhaled corticosteroids could have systemic effects, reaching the eyes and causing glaucoma.

They looked at Quebec residents 66 years of age and older — this is the group in which glaucoma is mainly seen — drawn from the health-insurance database. They compared the use of steroids between patients with glaucoma and randomly selected controls who did not have glaucoma and who had visited ophthalmologists in the same month as the case patients.

Although current use of inhaled or nasal steroids was *not* associated with an increased risk of ocular hypertension or open-angle glaucoma, use of high doses of inhaled steroids for 3 months or more *did* increase the risk.

Suissa explains that those at risk are the "10% of asthmatics considered to be severe, who take high doses of inhaled steroids maybe 8 times a day on a regular basis. We're not suggesting that inhaled steroids be withdrawn. These are extremely effective drugs for the treatment of asthma."

He suggests that older patients with severe asthma who are taking high-dose regimens of inhaled steroids be referred to an ophthalmologist, who can monitor ocular pressure and vision to ensure that any problems are recognized early. — C.J. Brown



Release of gelatinase A induced by platelet aggregation. Collagen caused concentration-dependent release of progelatinase A but not of gelatinase A (< 15 pg). Bars show means and standard deviations from 5 to 7 experiments, and the corresponding gel shows the data from a representative experiment. Reproduced with permission from *Nature* (1997;386:616).