

## Do dietary fatty acids affect platelet aggregation and arterial thrombosis tendency in a rat model?<sup>1,2</sup>


Gerard Hornstra and Johan Willem Marie Heemskerk

Dietary lipids affect arterial thrombosis in animal models (1, 2), but the mechanisms by which these effects are brought about are largely unknown. In this paper we discuss more recent studies that specifically address the relationship among dietary lipids, arterial-thrombosis tendency, and platelet aggregation.

Our rat model of arterial thrombosis is based on measuring the time (obstruction time, or OT, in hours) between insertion and complete thrombotic obstruction of a polythene, loop-shaped cannula, inserted into the abdominal aorta of male animals (3). Extensive validation of this model demonstrated that the results reliably reflect human arterial-thrombosis tendency. In a large series of studies of various vegetable oils ( $n = 19$ ) and oils and fats from marine ( $n = 8$ ) or terrestrial ( $n = 2$ ) animals, a strong, linear relationship was observed between the ratio of polyunsaturated to saturated fatty acids (P:S) of the dietary lipids ( $x$ ) and the relative OT (percent of value in animals fed sunflowerseed oil;  $y$ ):  $y = 95 + 24.6 \log x$ ,  $r = 0.71$ ,  $P < 0.001$ .

The slope of the relationship curve was significantly steeper for the marine lipids than for the terrestrial oils, which indicates that the antithrombotic effect of marine polyenes (polyunsaturated fatty acids, or PUFAs) may be more sensitive to the prothrombotic effect of saturated fatty acids (SFAs) than that of the terrestrial polyenes. Interestingly, collagen-induced platelet aggregation measured in citrated platelet-rich plasma, washed platelet suspensions, and citrated whole blood is not significantly correlated with OTs measured in animals fed the same diets. In addition, no such correlation was found when platelet aggregation (impedance) and ATP release (luminescence) were measured just before the start of thrombosis measurements in the same animals.

Diets that result in a reduced thromboxane formation in activated platelets tend to reduce both platelet aggregation in vitro and thrombosis tendency in vivo. However, good evidence has now been obtained that a reduction in platelet thromboxane production is associated with a higher sensitivity of these platelets for the prothrombotic activity of thromboxane (4), which largely offsets the putative beneficial effect of a reduced thromboxane formation. The same reciprocity seems to exist for prostacyclin (PGI<sub>2</sub>): in rabbits fed fish oil, PGI<sub>2</sub> synthesis is reduced but the sensitivity of platelets to the aggregation-inhibiting effect of PGI<sub>2</sub>

is enhanced. Hydrogenated coconut oil rich in SFAs, and therefore highly thrombogenic, invariably causes a lower collagen-induced platelet aggregation in vitro than more unsaturated, less thrombogenic, or even antithrombotic oils and fats, such as sunflower-seed oil (5). The aggregation reaction of rat platelets is extremely sensitive to small changes in extracellular calcium (1, 6), and the effects of dietary lipids on platelet aggregation in blood, anticoagulated with recombinant hirudin, are currently being studied. When platelet aggregation is measured in heparin-treated circulating arterial blood [by using the filter-loop technique (7)], spontaneous aggregation is invariably higher in the prothrombotic coconut-oil group than in the antithrombotic sunflower-seed-oil group. On the basis of these observations, the results of platelet aggregation studies in relation to arterial thrombosis tendency need to be reevaluated. 

### References

1. Hornstra G. Dietary fats, prostanoids and arterial thrombosis. Boston: Martinus Nijhoff Publishers, 1982.
2. Hornstra G. Influence of dietary fish oil on arterial thrombosis and atherosclerosis in animal models and man. *J Intern Med* 1989;225(suppl 1):53-9.
3. Hornstra G, Vendelmans-Starrenburg A. Induction of experimental arterial occlusive thrombi in rats. *Atherosclerosis* 1973;17:369-82.
4. Heemskerk JWM, Feijge MAH, Kalafusz R, Hornstra G. Influence of dietary fatty acids on membrane fluidity and activation of rat platelets. *Biochim Biophys Acta* 1989;1004:252-6.
5. Heemskerk JWM, Feijge MAH, Rietman E, Hornstra G. Rat platelets are deficient in internal Ca<sup>2+</sup> release and require influx of extracellular Ca<sup>2+</sup> for activation. *FEBS Lett* 1991;284:223-6.
6. Heemskerk JWM, Feijge MAH, Kester A, Hornstra G. Dietary fat modifies thromboxane A<sub>2</sub>-induced stimulation of rat platelets. *Biochem J* 1991;278:399-404.
7. Hornstra G. Method to determine the degree of ADP-induced platelet aggregation in circulating rat blood (filter-loop technique). *Br J Haematol* 1970;19:321-9.

<sup>1</sup> From the Department of Human Biology, Limburg University, Maastricht, The Netherlands.

<sup>2</sup> Address reprint requests to G Hornstra, Department of Human Biology, Limburg University, PO Box 616, 6200 MD Maastricht, The Netherlands.