Acute effect of high-fat meals rich in either stearic or myristic acid on hemostatic factors in healthy young men¹–³

Tine Tholstrup, Karsten Andreasen, and Brittmare Sandström

ABSTRACT  Suggestions have been made that saturated fatty acids with 12–18 carbon atoms, stearic acid (18:0) in particular, are prothrombogenic. These suggestions are based mainly on in vitro measurements. In the present study the effect of dietary fats high in stearic or myristic acid (14:0) on plasma triacylglycerol concentrations and key variables of blood aggregation (in vitro and in vivo), coagulation, and fibrinolysis was studied over 24 h in 10 healthy young men. For each dietary fat, two identical high-fat test meals were served: one in the morning (0 h) and one 8 h later, and blood samples were collected at 0, 2, 4, 6, 8, and 24 h. Both fats decreased platelet aggregation compared with fasting values. Stearic fat resulted in a tendency toward lower activity of plasminogen activator inhibitor 1 (PAI-1) than did myristic fat (P < 0.08). PAI-1 was also lower 24 h after consumption of either fat than initially (P < 0.05). Stearic fat, but not myristic fat, tended to cause some increase in factor VII coagulant activity and β-thromboglobulin after 4 h. In conclusion, an acute prothrombotic effect of fats high in myristic and stearic acid was not confirmed. Am J Clin Nutr 1996;64:168–76.

KEY WORDS  Stearic acid, myristic acid, aggregation, coagulation, β-thromboglobulin, fibrinolysis, plasma triacylglycerol

INTRODUCTION

Results from human intervention studies regarding markers of coronary heart disease are usually based on fasting blood samples. However, humans usually spend most of their day in a postprandial state. Intake of fatty meals may be regarded as a physiologic challenge; research has indicated that fatty meals play a role in coronary heart disease because postprandial lipoproteins appear to be atherogenic (1–3). Postprandial lipemia affects both the behavior and biochemistry of platelets (4), for which roles in coronary heart disease are well established (5). In addition, it was shown that blood coagulation activity is closely associated with the concentration of triacylglycerol-rich lipoproteins in plasma (6–8).

Early in vitro studies indicated that individual saturated fatty acids (SFAs) affect thrombogenesis (9–11). Connor (10) reported that stearic acid considerably shortened the thrombus formation time whereas unsaturated fatty acids had almost no effect. In Connor’s model, palmitic, myristic, and lauric acids were also prothrombotic but thrombogenicity decreased gradually with decreasing chain length. Several studies suggested that postprandial lipemia may increase platelet aggregation in humans (12–14). Acute platelet changes after meals high in SFAs have been suggested to increase the risk of arterial thrombosis (15). However, results are conflicting; other studies showed a decrease in aggregation or platelet activation after meals high in SFAs (dairy fat) (12, 13, 16). Because of discrepancies in the interpretation of results from aggregation studies, assessment of platelet activity on the basis of β-thromboglobulin is considered a more valid measurement of the in vivo situation. However, studies of the effects of postprandial lipemia on β-thromboglobulin are scarce (17, 18) and because of platelet activation ex vivo the results may be difficult to interpret (19).

Fibrinolytic variables vary diurnally in a characteristic inverted-U shape for t-plasminogen activator (t-PA) activity and in a U shape for plasminogen activator inhibitor 1 (PAI-1) activity (20), but changes in type of test fat in the diet do not affect the fibrinolytic variables. Others showed an association between PAI-1 activity and fasting triacylglycerol concentrations (21) and observed a steeper decline of PAI-1 activity after consumption of an fat-free meal than a meal containing fat (19). In summary, studies of the effect of individual fatty acids on postprandial lipemia and changes in hemostatic variables are few and the results are contradictory.

In a previous study with dietary periods of 3 wk we showed that feeding a high–stearic acid test fat to healthy young men lowered factor VII coagulant (factor VIIc) activity, as analyzed in fasting blood samples, compared with the effects of fats high in palmitic or myristic and lauric acids (22). In the present study of healthy young men, we monitored over 24 h the acute

¹ From the Research Department of Human Nutrition, the Royal Veterinary and Agricultural University, Copenhagen, and the Coagulation Laboratory, Department of Clinical Chemistry, Gentofte Hospital, University of Copenhagen, Gentofte, Denmark.
² Supported by the Danish Agricultural Ministry (grant RAA92-KVL5), the Danish Agricultural and Veterinary Research Council (grant 13–4685–1), and the Danish Technical Research Council (grant 16–5034–1).
³ Address reprint requests to T Tholstrup, Research Department of Human Nutrition, The Royal Veterinary and Agricultural University, Rocihgsvej 30, DK-1958 Frederiksberg, Denmark. E-mail: nn@kvl.dk or Tine.Tholstrup@hje.kvl.dk.
Received December 8, 1994.
Accepted for publication April 30, 1996.

effect on hemostatic variables of meals high in stearic acid (stearic fat) or myristic acid (myristic fat). For each fat, identical high-fat test meals were served at 0 and 8 h. Our aim was to investigate a possible association between lipemia and key variables of blood aggregation, coagulation, and fibrinolysis.

SUBJECTS AND METHODS

Subjects

Ten young men were recruited for the study. They were between 21 and 28 y of age (x̄: 23 y), weighed from 68 to 101 kg (x̄: 81 kg), and had body mass indexes (kg/m²) from 21 to 29 (x̄: 24). None had any history of atherosclerotic disease and they were all apparently healthy as indicated by a medical questionnaire. They were all nonsmokers. None had hypertension or was taking any medication. Most of them performed moderate amounts of physical activity (training a maximum of 1–2 h twice a week, daily cycling to work, or both). The protocol and aim of the study were fully explained to the subjects, who gave their written consent. The research protocol was approved by the Scientific Ethics Committee of the municipalities of Copenhagen and Frederiksborg (01296/93).

Diets

Two different high-fat test meals (containing either stearic or myristic fat) were served in random order to each man. The two intervention periods were separated by ≥ 8 d of consumption of the subjects’ habitual diets. Each study period was 24 h and included two identical meals, one consumed in the morning after the 0-h blood sample was drawn and one in the afternoon after the 8-h blood sample was drawn.

Food was prepared and individual servings were weighed at the experimental kitchen of the Department of Human Nutrition of the Royal Veterinary and Agricultural University. The dishes were served to the subjects at the Coagulation Laboratory, Gentofte Hospital, Department of Clinical Chemistry, where the subjects stayed until after they consumed the second meal. After this, the subjects could have only water until the next day after the second fasting blood sampling (24-h sample) was drawn.

The meal included test fat–enriched rolls and cakes plus juice and marmalade. Each participant’s energy requirement was individually estimated according to weight, sex, age, and level of physical activity (23). The fat content of each test meal was fixed at 1.2 g/kg body wt. Fifty-two percent of the energy contribution was from fat, 44% from carbohydrates, and 4% from protein. The energy content of each test meal ranged from 5.9 to 8.8 MJ (x̄: 7.0 MJ) and fat content of each test meal ranged from 82 to 121 g (x̄: 97 g).

A high–stearic acid test fat (stearic fat) and a high–myristic acid test fat (myristic fat) were used to achieve the desired differences in fatty acid composition. Both fats were provided by Aarhus Olie (Oils and Fats Division, R&D, Aarhus, Denmark). The fatty acid composition of each test fat was determined through use of gas-liquid chromatography (Table 1). The positional distribution of the fatty acids in the triacylglycerols of the two fats was determined through use of an HPLC method (analyzed by the laboratories of Aarhus Oliefabrik A/S, Aarhus, Denmark). Shea butter (the kernel fat of the shea butter tree, Butyrospermum parkii, Sapotaceae), a fat used for cooking and frying in Nigeria, was used as the stearic fat. The shea butter was a refined product and was rinsed with acetone to remove nonsaponifiable compounds. The content of nonsaponifiable compounds in the shea butter was 6.9%. The composition of these shea butter compounds was not analyzed except for the keratine content, which was 0.74%. As expected, stearic acid was exclusively in the α position. The myristic fat was synthetic and made especially for this study by interesterifying trimyristin, a commercial fat containing 98.2% myristic acid (Dynasan 114; Hüls, Marl, Germany), with high-oleic acid sunflower oil (a commercial fat, TRISUN 80; SWO Enterprises, Eastlake, OH). As expected, myristic acid was equally distributed between the α and β positions. The two test fats were not analyzed or balanced for nonglyceride constituents such as tocopherols and tocotrienols.

Blood sampling and analysis

Morning blood samples were taken on day 1 (0 h) and day 2 (24 h) of each test period after ≥ 12 h of fasting and after 20 min of supine rest. Subjects refrained from alcohol intake and heavy physical activity for ≥ 24 h before sampling and were told to get to the hospital for the morning sampling in a nonstrenuous way, i.e., not to run or bike to the hospital. In between blood drawings the subjects pursued their usual study activities or walked around in the hospital area. Postprandial samplings were taken 2, 4, 6, and 8 h after the beginning of the meal on the first day. Blood for triacylglycerol determination was collected in tubes containing EDTA. Blood samples for the measurement of factor VIIc, t-PA, and PAI-I activity were collected in citrated tubes. Blood for β-thromboglobulin analysis was collected as a second sample in Diatube H tubes (Diagnostica Stago, Asnieres sur Seine, France) containing an anticoagulant mixture and with the vacuum already broken. Samples were immediately placed on ice for ≥ 15 min and were centrifuged for 30 min at 3000 × g at 4 °C (model TJ-R; Beckman Instruments, Fullerton, CA). After centrifugation, one-third of the plasma supernate (platelet-poor plasma) was carefully collected and stored at −38 °C. Triacylglycerol concentrations were assessed by enzymatic procedures (Boehringer Mannheim GmbH, Mannheim, Germany) with a Cobas Mira analyzer (Roche, Basel, Switzerland). The plasma concentration of C-reactive protein was assessed to check if any subjects harbored infectious diseases during the period of blood collection. Values were in the normal range (< 40 nmol/L) except in one subject in whom the concentration was 41 nmol/L.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Fatty acid composition of test fats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatty acids</td>
<td>Myristic fat</td>
</tr>
<tr>
<td>% of total test fat</td>
<td></td>
</tr>
<tr>
<td>≤ 10.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Lauric acid</td>
<td>0.1</td>
</tr>
<tr>
<td>Myristic acid</td>
<td>43.0</td>
</tr>
<tr>
<td>Palmitic acid</td>
<td></td>
</tr>
<tr>
<td>Stearic acid</td>
<td>2.5</td>
</tr>
<tr>
<td>Oleic acid</td>
<td></td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>10.5</td>
</tr>
<tr>
<td>Linolenic acid</td>
<td>0.1</td>
</tr>
<tr>
<td>≥ 20.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>
**Blood for coagulation and fibrinolysis**

Plasma factor VIIc (% was assessed with a clotting assay. Test plasma was added to plasma deficient in factor VII (Baxter Diagnostics AG, Didingen, Switzerland). Thromboplatin and Ca²⁺ (Instrumentation Laboratories, Milano, Italy) were added to induce clotting, and the clotting time was measured. Factor VIIc was calculated by reference to a standard graph produced by testing dilutions of a human plasma (standard; Diagnostics AG) with the same method. t-PA activity (pmol/L) was determined through use of a solid-phase immunosorbent assay (Novo Nordisk A/S, Bagsværd, Denmark) involving 1) coating of wells in microtiter plates with a monoclonal antibody directed toward an epitope on t-PA apart from the active site, 2) binding of t-PA to a solid-phase antibody, and 3) activation of plasminogen by antibody-bound t-PA in the presence of a potent stimulator. The procedure was described previously (24). PAI-1 activity and the t-PA-PAI-1 complex (pmol/L) were estimated by a double monoclonal immunoenzymatic assay with peroxidase as the enzyme (Novo Nordisk A/S). The chromogenic reaction was measured photometrically. A further description was given previously (25).

β-Thromboglobulin was assessed with a commercial enzyme immunoassay kit (Asserachrom; Diagnostica Stago) (26). Values higher than the normal range of < 60 × 10^3 U/L were excluded because higher values indicate poor blood sampling and handling. We excluded six samples from three persons.

**Platelet aggregation studies**

Blood for the platelet aggregation studies was collected in citrated tubes and centrifuged in a Beckman TJ-6 centrifuge (Beckman Instruments) for 15 min at 100 × g at 18 °C (900 rpm). The resulting platelet-rich plasma was carefully removed and stored at room temperature for 30 min. The remainder was further centrifuged for 10 min at 1500 × g at 18 °C (2600 rpm) to obtain platelet-poor plasma. Platelet aggregation studies were performed with an aggregometer (platelet aggregation profiler PAP-4; BIO/DATA, Medionova, Denmark) with microcuvettes at room temperature (37 °C) and with a stirrer speed of 1000 rpm. The light transmission of the aggregometer was adjusted before each experiment with platelet-rich and platelet-poor plasma to 100% and 0%, respectively. Aggregation was recorded for 5 min. Platelet-rich plasma was preincubated at 37 °C for 2 min before aggregation was triggered by the addition of collagen to final concentrations of 1, 5, and 10 mg/L and of ADP to concentrations of 1, 5, and 10 μmol/L. ADP was dissolved in 0.9% NaCl and stored in small plastic test tubes at −20 °C before use. Collagen reagent (HORM; Nycomed, Arzneimittel GMBH, Garching-Hochbruck, Germany) was freshly diluted with HORM buffer before each experiment. The study was planned so that each experimental aggregation began 40 min after blood collection and lasted for 30 min. We excluded seven lipemic samples because of turbidity. Samples were excluded if the aggregation did not exceed 50% after stimulation with 10 mg collagen/L or 10 μmol ADP/L.

**Statistical analysis**

Repeated-measures analysis of variance (SPSS Inc, Chicago) with Huynh-Feldt adjustment of degrees of freedom was used to assess effect of time, difference in effect of the experimental fats, and interaction between effects of time and type of fat during the 0–8-h period of the day. For a significant interaction between effects of time and type of fat to be found, the mean difference between the two fats must vary with time. Graphs of the time course were used to illustrate how the means differ. For significant interactions, tests for type of fat and time effects are not meaningful and are therefore not reported. If, however, there was no significant interaction, the two time courses can be regarded as parallel and the effects of time and type of fat can be tested separately. The test for effect of type of fat is then a test of the null hypothesis that the two time courses are equal, and the test for effect of time is a test of the hypothesis that concentrations are constant over time. The paired t test or Wilcoxon test was used to compare baseline concentrations before (0 h) and 24 h after the test meal.

**RESULTS**

The high-fat meals rich in either stearic or myristic acid caused a considerable increase in plasma total triacylglycerol (Figure 1). Aggregation activity decreased and reached a minimum after 4 h (Figure 2, A, C, and E and Figure 3, A, C, and E). Fibrinolytic activity increased and reached a maximum after 8 h (t-PA, Figure 1) and PAI-1 activity and t-PA–PAI-1 complex decreased to their minimum after 8 h (Figure 1).

There was no significant difference in the time course of total triacylglycerol concentrations after the two different test fats nor in the mean total triacylglycerol concentration according to the repeated-measures analysis of variance. There was, however, a significant variation with time (P < 0.01) (Figure 1). Because baseline concentrations of β-thromboglobulin tended to differ, although not significantly, the differences (Δ values) between values 4 and 8 h after intake of the test fats and the initial value at 0 h were analyzed. The Δ values of β-thromboglobulin did not show any interaction effect (time by type of fat), but the effect of time was significant (P < 0.05) (Figure 1). For factor VIIc the interaction effect was not significant during the 0–8 h period. From Figure 1 it appears that there was a tendency for factor VIIc to increase from 4 to 8 h after consumption of the stearic fat, whereas there was hardly any change after consumption of the myristic fat. t-PA activity increased during the 0–8-h period (P < 0.01) (Figure 1). PAI-1 activity decreased during the 0–8 h period (P < 0.01) and tended to be lower after consumption of stearic fat than myristic fat (P = 0.08). In addition, when concentrations of PAI-1 at 0 and 24 h were analyzed, the mean values were lower at 24 h than before the intake of the test fats (P = 0.054) (Figure 1). The t-PA–PAI-1 complex decreased significantly with time during the 0–8-h period (P < 0.05) (Figure 1).

Aggregation activity induced by 1 mg collagen/L was not different by time or between test fats over the period from 0 to 8 h (Figure 2A). Comparisons of the 0- and 24-h concentrations showed a lower value after consumption of stearic than myristic fat (P = 0.02). The slope induced by 1 mg collagen/L decreased during the 0–8-h period (P < 0.001) (Figure 2B). Aggregation activity induced by 5 mg collagen/L decreased during the 0–8-h period (P < 0.01) and tended to be lower after consumption of stearic fat than myristic fat (Figure 2C). The slope induced by 5 or 10 mg collagen/L decreased during the 0–8-h period (P < 0.001) (Figure 2, D and F).
Aggregation activity induced by 1 μmol ADP/L was not different (Figure 3A). The slope induced by 1 μmol ADP/L decreased during the 0–8-h period ($P < 0.001$) (Figure 3B). Aggregation activity induced by 5 or 10 μmol ADP/L decreased during the 0–8-h period ($P < 0.001$) (Figure 3, C and E), whereas the slope induced by 5 or 10 μmol ADP/L showed interactions between time and type of fat ($P < 0.005$) (Figure 3, D and F).
FIGURE 2. Entry values before fat load and changes after intake of myristic fat (solid lines and circles) and stearic fat (dashed lines and crosses) in collagen aggregation activity and the slope induced by 1 (A and B), 5 (C and D), and 10 (E and F) mg collagen/L, respectively. Samplings at 0 and 24 h are fasting values, other values are postprandial. $\bar{x} \pm$ SEM; $n = 10$. 
FIGURE 3. Entry values before fat load and changes after intake of myristic fat (solid lines and circles) and stearic fat (dashed lines and crosses) in ADP aggregation activity and the slope induced by 1 (A and B), 5 (C and D), and 10 (E and F) μmol ADP/L, respectively. Samplings at 0 and 24 h are fasting values, other values are postprandial. \( \bar{x} \pm \text{SEM}; n = 10. \)
DISCUSSION

The general purpose of this study was to increase our understanding of two dietary SFAs in regard to thrombogenesis. Acute effects of selected variables in the hemostatic system and in vitro platelet aggregation were studied in healthy young men after they consumed meals high in stearic or myristic acid.

The acute effects of feeding stearic fat on the degree of collagen- and ADP-induced platelet aggregation were not different from those of feeding myristic fat, and the degree of platelet aggregation induced by both collagen and ADP decreased after both fats. The decrease in aggregation as shown in this study is in contrast with a suggested prothrombotic role of these SFAs (27–30) and with some results showing increased platelet aggregation after high intakes of SFAs (31–33). However, decreased aggregation or platelet activation after a fat load has also been observed (12, 34). Furthermore, one study showed that palmitic and stearic acids in phospholipids are associated with decreased collagen-induced platelet aggregation (35).

Part of the discrepancy in the interpretation of the effects of a fat load on aggregation has been suggested to be due to the different techniques used. Bisovsky et al (36) and Sinzinger et al (37) showed that as opposed to platelet-rich plasma, washed platelets increased collagen and ATP aggregation after fat intake (36, 37). For aggregation studies with platelet-rich plasma and washed platelets, it was argued that a selection of certain platelet subpopulations may take place during differential centrifugation. Furthermore, the possible contribution of leukocytes and erythrocytes to aggregation is excluded (38). For that reason, measurement in whole blood is preferred by some (38). A study of whole blood and platelet-rich plasma (by using the impedance method) showed an inhibitory effect on platelet activation caused by an increase in chylomicrons after fat intake (12). These inconsistencies indicate a need for additional methods with which to investigate platelet aggregation.

Regarding mechanism, it was suggested that an observed enhancing effect of rapeseed and sunflower oils on platelet aggregation (in contrast with the effect of milk fat), observed in fasting values after intake of test diets for weeks, was due to changes in thromboxane production (39). This effect is not likely to have played a role in our study, because it has been shown that SFAs do not affect postprandial prostanooid metabolism (13). A more probable mechanism in our study is chylomicron coating of the platelet. This phenomenon was shown in electron microscopy studies with fat infusion in humans (40). A fat coating might cause the aggregation to decrease because it may interfere with the platelet-collagen interaction that takes place in the initial stage of platelet activation (12). This hypothesis is in agreement with a depressed platelet function in patients with type V hyperlipoproteinemia (41). However, it remains uncertain whether this suggested in vitro mechanism can be applied to an in vivo situation.

Because of the controversy over the interpretation of in vitro aggregation results and the lack of a human model for arterial thrombosis, we measured the release of the platelet-specific protein plasma β-thromboglobulin. This method is considered to be a more valid, indirect way of interpreting the in vivo behavior of platelets (38). However, many results obtained by measuring the release of β-thromboglobulin are vague and difficult to interpret because, among other things, assessment of platelet activity on the basis of β-thromboglobulin is associated with technical difficulties (42). Platelets are easily activated during blood sampling and handling (19). As a result, part of the β-thromboglobulin data is excluded during reporting, thereby obscuring the results. In our study, β-thromboglobulin tended to increase after consumption of stearic fat, whereas it decreased slightly with consumption of myristic fat. The pattern in effect of test fats on platelet aggregation was not reflected in the effect on β-thromboglobulin. This observation seems to indicate that the decrease in aggregation in our study originated from mechanisms different from those causing the change in β-thromboglobulin. This finding may support the hypothesis that the observed antiaggregation is due to an interaction at an earlier stage of platelet activation. This apparent anticoagulative effect after loads of SFAs may represent a physiologic defense mechanism against a possible thrombogenic effect of SFAs, a mechanism that has also been suggested by others (10, 30).

The effect of time and test fat on factor VIIc appears to be a delayed increase after intake of stearic fat and an unchanged concentration after intake of myristic fat. The effect on factor VIIc tended to be similar to the effect on β-thromboglobulin. Thus, it can be hypothesized that the regulation mechanisms are related. The ambiguous effect on factor VIIc does not agree with results by others, who found a clear procoagulatory change in factor VIIc after high fat intakes (43–46). In addition, it has also been suggested that the plasma stearic acid concentration induces a higher factor VIIc activity than do plasma palmitic, oleic, and linoleic acids (47). However, the plasma stearic acid concentration has been shown to be poorly related to intake of dietary stearic acid (48). Other studies showed that fatty acids have similar procoagulatory effects (19, 44). The reason for these discrepancies may lie in the different compositions and amounts of fats used and in the different methods of these studies. In our study, factor VIIc could have increased further after the measurement at 8 h, because of a slower gastric emptying after high fat intake. Thus, we may not have observed the peak value. It should be emphasized that the test fats used in our study, which were dominated by one single SFA, differ considerably in fatty acid composition from the test fats used by others and that contained mixtures of SFAs. In addition, the nonglyceride components of stearic fat (shea butter) in our study may have influenced the results.

PAI-1 activity has a strong diurnal variation (49) and is inversely associated with triacylglycerol concentration (21), an observation that is consistent with our findings (20). Although it has been suggested that PAI-1 activity is not affected postprandially by dietary changes (49), we observed a tendency for PAI-1 activity to be lower during the 8 h after intake of stearic fat than after myristic fat. In addition, PAI-1 activity was lower after the 24-h test period compared with initial values. These results could either be an effect of the test fats or reflect the initiation of a diurnal decrease after the fasting period of 14 h. A relation between fasting triacylglycerol concentration and PAI-1 was observed by others (21). In addition, a recent study showed that "remnant-like particles" can stimulate the secretion of PAI-1 by cultured endothelial cells (50).

Our study showed a positive association between initial plasma triacylglycerol concentrations and peak plasma triacylglycerol concentrations. Thus, subjects with higher initial values responded more to the test fats than did subjects with lower
values. This result is in agreement with findings reported by others (51–54).

Absorption of stearic acid has been argued (55–57). In our study there was a tendency for a lower triacylglycerol concentration after consumption of stearic fat compared with myristic fat after 2 h (Figure 1). This might be due to a slower initial absorption ratio of stearic fat. After 4 h the plasma triacylglycerol concentration was identical with the two test fats (Figure 1). In addition, the content of stearic and myristic acids (after 4 h) did not differ in the chylomicrons in five of six person investigated (data not presented). Thus, stearic and myristic acids may be equally absorbed after 4 h. This finding agrees with results by others who showed that fats high in stearic acid were well absorbed (58, 59).

In conclusion, the acute effects of stearic and myristic acids on factor VIIc and β-thromboglobulin suggest that the anticoagulative effects observed are due to an earlier stage of platelet activation. Furthermore, because of the inconclusive effects of stearic and myristic acids on factor VIIc and β-thromboglobulin, further studies are needed to clarify our understanding of thrombogenesis, factors that affect it, and their mechanism or mechanisms of action.

We sincerely thank Peter Markmann for his advice and comments. We thank Aarhus Oliefabrik A/S, Oils and Fats Division, R&D, Denmark, for analysis and delivery of test fats. We are also grateful to the staff at the Coagulation Laboratory at Gentofte Hospital for their enthusiasm and excellent work. We especially thank Bo Jacobsen, Mette Jørgensen, and Hanne Skovmøller.

REFERENCES

35. Kwon J-S, Snoek JT, Wardlaw GM, Hwang DH. Effects of diets high in saturated fatty acids, canola oil, or safflower oil on platelet function,