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DIETARY LIPIDS, INFECTION AND MACROPHAGE PROCOAGULANT ACTIVITY.
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It is generally accepted that the type of dietary fat influences arterial thrombosis and atherosclerosis. Although it is still largely unknown how the dietary lipid composition influences the process of atherogenesis, it is evident that several cell types are involved. Morphological evidence for the involvement of monocyte/macropages has been given.
We described before that the dietary lipid composition has striking effects on the procoagulant activity of macrophages. When macrophages were isolated from the spleens of healthy rats the procoagulant activity slightly decreased during the first few hours after isolation, and reached a plateau value after 4 hours. When, however, macrophages were obtained from animals infected with a pneumona virus (PVM) different results were obtained:

dietary lipid	healthy animals MØ PCA 24 h Clot.time (s)	PVM-infected animals MØ PCA 1 h Clot.time (s)	MØ PCA 24 h Clot.time (s)
5en% PPC	100.4 ± 6.2	69.6 ± 6.1	54.3 ± 4.3
5en% SO	74.2 ± 0.4	57.2 ± 6.7	52.4 ± 4.3
50en% SO	73.8 ± 1.6	59.5 ± 9.3	48.1 ± 5.0

PPC:Polyene phosphatidylcholine from soybean;SO:sunflowerseed oil

Experiments carried out with peripheral blood monocytes showed close resemblance to those described in the table.
These results show that:
- moncytes/macrophages isolated from PVM-infected animals increase their procoagulant activity during in vitro culture
- the differences in macrophage procoagulant activity found in cells obtained from healthy animals fed diets containing different lipids no longer were found in PVM-infected animals.

This would implicate that the infection process has a more profound influence on macrophage procoagulant activity that the composition of the diet.

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HYPERCOAGULABILITY AND REDUCED SENSITIVITY TO WARFARIN IN RATS FOLLOWING CAFFEINE INTAKE. M. Gerna, M.B. Donati, Istituto Mario Negri, Milano, Italy

The effect(s) of caffeine intake on cardiovascular functions are still a matter of debate. We have considered here the level of the prothrombin complex activity as a parameter of blood coagulability following caffeine intake. The activity of the four vitamin K-dependent clotting factors (II, VII, IX and X) was tested after acute and chronic administration of high doses of caffeine. With a single administration of 50 mg/kg caffeine a statistically significant increase in the activity of factors VII, IX and X was observed. The increase lasted for 4, 3 and 2 days respectively. Factor II was not affected by caffeine administration. The same effect was observed during chronic administration (50 mg/kg/day). With a lower dose of caffeine during chronic administration (5 mg/kg/day) only factor X showed a significant increase. A single dose of caffeine (50 mg/kg) given to animals 24h before a dose of warfarin (0.4 mg/kg i.v.) markedly reduced the anticoagulant effect of warfarin, as measured by the thrombotest. During the latter experiment we measured also the rate of synthesis (Rsyn) of the prothrombin complex activity. Rsyn, during warfarin treatment, was significantly higher in the rats pretreated with caffeine than in controls. γ-Carboxylase activity in rat liver microsomes was measured after administration of 50 mg/kg of caffeine as a single dose. The incorporation of $^{14}CO_2$ in the endogenous precursor was higher in the rats pretreated with caffeine than in controls (84,905 cpm/mg of protein versus 59,826 cpm/mg of proteins); this difference, however, was not statistically significant. In conclusion, caffeine intake may affect the clotting system mainly by stimulating the synthesis of factors of the prothrombin complex and, as a consequence, their response to coumarin anticoagulation.

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VITAMIN K_1 IN HUMAN MILK. R. v. Kries (1), M.J. Shearer (2), P.T. McCarthy (2), M. Haug (3) and G. Harzer (3).
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Fatal vitamin K deficiency haemorrhage has been observed in breast fed babies. Though the incidence of vitamin K deficiency haemorrhage seems to be low in exclusively breastfed babies in Germany, subclinical vitamin K deficiency is by far more common as demonstrated in recent studies. Vitamin K concentrations in human milk are lower than in cow's milk and infant formula, however, nothing is known about the factors determinating the vitamin K concentrations in human milk. Vitamin K_1 concentrations in human milk were studied during the first five weeks of lactation with respect to a) stage of lactation, b) interindividual differences, c) relationship of vitamin K_1 to other lipids, and d) influence of oral supplements of vitamin K_1 given to the mother. Milk samples from 9 mothers were collected on day 1,3,5,22,29 and 36 of lactation using standarized techniques.
a) Vitamin K_1 concentrations in colostral milk, day 1-5 (median 1,8 ng/ml) were significanctly higher than in mature milk, day 22-36 (median 1,1 ng/ml) (Wilcoxon U-Test $p < 0,01$). These changes during the course of lactation must be considered for estimation of the vitamin K supply in breastfed babies.
b) Vitamin K concentrations both for colostral and mature milk were found to vary widely: colostral milk 0,6-4,4 ng/ml, mature milk 0,4 - 2,8 ng/ml.
c) For colostral milk regression analyses revealed good correlations of vitamin K_1 to cholesterol but none to total lipid and phospholipids, whereas no correlation to either lipid was observed for mature milk. Cholesterol appears to have a role in vitamin K_1 secretion into colostral milk.
d) Vitamin K_1 concentrations of maternal milk were influenced by oral supplements given to the mother. Even with a dose of 100 µ vitamin K_1 (similar to the dose which may be ingested with a meal) a twofold increase of the vitamin K_1 content of breast milk was observed. These data suggest that mutritional factors may influence the vitamin concentration in human milk. Vitamin K supplements for breastfeeding mothers on vitamin K_1 poor diets could improve the vitamin K supply of these babies.

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SERUM PREPARED AFTER DAILY INTAKE OF FISH INHIBITS PGI-2 PRODUCTION BUT NOT PLATELET INHIBITORY ACTIVITY OF ENDOTHELIAL CELLS. T. Simonsen (1), Å. Vårtun (1), V. Lyngmo (1), G. Hornstra (2) and A. Nordøy (1). Dept. of Medicine, University Hospital, Tromsø, Norway (1) and Dept. of Human Biology, Limburg, Maastricht, The Netherlands (2).

Healthy males were given dietary supplement of 100 g mackerel pasta for six weeks. Controlls were given meatpasta. Blood were collected before and at the end of the dietary intervention. Fatty acid composition of total phospholipids in serum and free fatty acids were measured by GLC.

Human endothelium cells were grown in medium supplemented with 10% serum prepared from blood of the mackerel and controll groups. The medium was then examined for PGI-2 by RIA of 6-Keto-$PGF1_\alpha$, and for platelet aggregation inhibitory activity (PAIA) measured as inhibition of collagen induced platelet aggregation in platelet rich plasma.

Fatty acids of total phospholipids and FFA of serum showed a significant decrease in the ratio of Arachidonic acid (20:4 n-6) to Eicosapentaenoic acid (20:5 n-3) in the mackerel group.

The 6-Keto-$PGF1_\alpha$ was significantly lower in the medium added serum from the mackerel group at the end of the period than at start. PAIA was not reduced by serum collected after fish consumption.

We conclude that dietary fish contribute to factors in serum, inhibiting PGI-2 production in endothelial cells in vitro. However, the ability of endothelial cells to inhibit platelet aggregation was not affected.