entered the study groups A and B had the test positive. Blood samples were collected during 60–90 seconds after the patient had achieved fixed diagnostic symptoms of ischaemia.

All pts in group A were treated with enalapril and some – with indapamide, statins and betablockers (mean blood pressure 132/96 mmHg); these pts and pts in group B (mean blood pressure 122/84 mm/Hg) were also given nitrates and aspirin. Control group (C) consisted of 20 healthy normotensive volunteers (test negative). All parameters were examined in plasma using commercialy available kits.

Results:

Study group	TF IU/ml	TAT ng/ml	F 1 + 2 nmol/L
A	422±121	2.4±1.3	0.78±0.28
B	405±104	2.2±1.1	0.65±0.23
C	379±130	2.0±1.4	0.56±0.30

$p < 0.05$ for TF, TAT and F1 + 2 in A vs C

Conclusions: Patients with PH and IHD release statistically more TF and generate more thrombin while exercise tested than controls; there is no difference in examined parameters in IHD pts with PH versus IHD without PH as well as in pts with IHD alone versus healthy controls.

P358 DIMEPHOSPHONE EFFECT ON VESSEL WALL ANTIAGGREGATING POTENTIAL

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Previously we have shown a direct inhibitory effect of dimephosphone (Dph) – the dimethyl ether of 1,1-dimethyl-3-oxobutylphosphonic acid, on platelet aggregation. It is generally accepted that platelet aggregation in vivo is regulated by the multiple factors originated from vascular endothelium, especially prostacyclin and NO. The aim of this study was to investigate the ability of Dph to affect antithrombotic properties of vessel wall in vitro. The study was carried out on freshly isolated rat aortic strips. The strips were incubated in № 199 medium for 20 min in the presence of 100, 500 mkM Dph or without Dph. The tissue was removed and the antiaggregating properties of supernatant were tested according to their ability to inhibit platelet aggregation in platelet rich plasma (PRP) triggered by 5 mkM ADP. Aggregation rates in native PRP samples obtained from healthy volunteers were referred to as control. Taking into account the phenomenon of cold-induced platelet activation, we performed the study with (1) and without (2) short-term exposition of PRP to low temperature. In group 1 platelet aggregaion to ADP was increased by 100% and was not inhibited by vascular metabolits in Dph-free supernatant. Dph in concentration 100 mkM also didn't affect platelet aggregation. However, aggregation rate showed decline towards the control level in the presence of 500 mkM Dph ($p < 0.05$).

Table 1. Platelet aggregation rate (%) to 5 mkM ADP

group	control PRP	PRP + supernatant		
		no Dph	100 mkM Dph	500 mkM Dph
1	100	201.7±24.8 (p<0.01)	196.1±27.7	107.8±12.5 (p<0.05)
2	100	39.6±3.5 (p<0.01)	72.2± 11.4 (p<0.05)	40.8±5.2

In group 2 platelet aggregation rate was inhibited by 60% comparing to the control by the active metabolits, released from the vessel wall in the absence of Dph. In contrast, preincubated with 100 mkM Dph aorta samples induced smaller changes in the platelet response to ADP that was attributed to the ability of Dph to suppress the antiaggregating potential of the vessel wall. In concentration 500 mkM Dph besides inhibiting platelet aggregation also acted as an inhibitor of the endothelial cells and thus produced a stimulating effect on platelet aggregation. As a result of this dual action the final aggregation rate did not change. These data demonstrate, that the resulting effect of Dph in complex systems would depend on the rate of aggregation and on the initial functional state of target cells.

Since its direct inhibitory effect on platelets is rapidly developed, we can assume that Dph would also produce fast inhibition of platelet aggregation in acute clinical situations. As far as its action extends to endothelial cells, its antiaggregating effect may become less potent.

20. Triglycerides

P359 THP-1 FOAM CELLS RESPOND TO A TRIGLYCERIDE RICH LIPOPROTEIN MEDIATED REDUCTION IN CHOLESTEROL EFFLUX BY INCREASING CHOLESTEROL BIOSYNTHESIS

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Type II diabetes, and associated increased incidence of atherogenesis, is characterised by high circulating levels of triglyceride rich lipoprotein (TGRL). TGRLs are established as independent risk factors for coronary artery disease but the mechanisms involved are as yet unclear. We propose that accumulation of TGRLs within macrophage foam cells contributes to their role in plaque formation, and in particular, impedes the ability of these cells to effectively expel excesses of intracellular cholesterol.

Human (THP-1) macrophages were loaded with acetylated (ac) LDL for 48 h to induce substantial cholesterol loading and labelled with ^{3}H-cholesterol as a tracer for cholesterol efflux. These foam cells were then incubated with TGRL (50 μg/ml, 24 h), washed and incubated with apolipoprotein (apo) A1 (10 μg/ml, 24 h) to induce cholesterol efflux. An impairment of cholesterol efflux was observed in TGRL-loaded foam cells compared to controls loaded with BSA-medium alone (TGRL 5.4±0.62 υ control 8.5±1.0%; $n = 4$, $p < 0.05$). In contrast, native (non acLDL loaded) macrophages did not exhibit TGRL-mediated impairment of cholesterol efflux. This inhibition of cholesterol efflux was exacerbated by a lack of mobilisation of cholesterol ester (CE) stores, as indicated by a lack of alteration in ^{3}H-oleate labelled CE in response to apoA1 (control 6.3±0.6 υ apoA1 6.4 ± 0.3 nmoles/mg protein, $n = 3$). This lack of CE mobilisation was also apparent in TGRL-incubated cells (control 6.2±0.5 υ apoA1 5.7±0.8, $n = 3$). Foam cells responded to this TGRL-mediated decrease in cholesterol efflux by stimulating cholesterol synthesis, as measured by increased incorporation of ^{14}C-acetate into cellular free cholesterol (TGRL [50 μg/ml] 19.1±3.0 υ control 8.8±1.4 10^3 counts, $n = 3$, $p < 0.05$). An identical effect was observed in both control and apoA1 efflux conditions. These data provide intriguing insights into the deleterious consequences of high TGRL in reverse cholesterol transport but further experiments are required to deduce the mechanisms by which they exert these effects.

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P360 EFFECT OF DIET INTERVENTION ON LONG TERM MORTALITY IN HEALTHY HYPERLIPIDEMIC MEN

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The aim was to study the effect of 5 years diet intervention on 24 years mortality in hyperlipidemic middle aged men..

We studied 104 healthy men aged 40–49 years with baseline values of total serum cholesterol > 7.75 mmol/l and fasting triglycerides > 2.95 mmol/l, within the randomised diet and smoking cessation trial of the Oslo study ($n = 1232$). In this trial the participants were randomised to a diet intervention or control group for 5 years. The diet consisted of a traditional lipid lowering diet with emphasis on reduction of saturated fat and body weight. The groups were well balanced with regard to traditional risk factors for mortality.

33 subjects died during the 24 years observation period.

In the diet intervention group, mortality was reduced by 51% (RR = 0.49, $p = 0.022$) as compared to the control group.

This difference remained significant in a Cox regression analysis after adjusting for age and smoking (RR = 0.47, $p = 0.038$).

Diet intervention	Yes	No
n	55	49
mortality %,	21.8	42.9

p = 0.022

This study indicates that the investigated 5 year diet intervention reduces late mortality in healthy hyperlipidemic men.

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