Introduction

The triglyceride molecule has been in the focus for lipidologists from the middle of the last century upon the development of the ultracentrifuge separation method (Havel *et al.* 1955) which has been applied in lipoprotein and atherosclerosis research on a worldwide basis ever since. Although a conclusive large-scale epidemiology study was not available, Dan Zilversmit has formulated a strong opinion that triglyceride concentrations of chylomicrons and very low-density lipoprotein remnant particles play a substantial role in atherosclerosis development (Zilversmit 1995). This idea has seen further research directed toward changes in triglyceride-rich lipoprotein composition, their remnants, and increased triglyceride content in the liver (Piťha *et al.* 2015, Vrablík and Češka 2015).

Subsequently, larger clinical studies have documented a link between triglyceride intravasal concentration and coronary heart disease risk (Hokanson and Austin 1996), even though in some studies this significant effect has been ruled out after adjustment for HDL cholesterol concentrations. This phenomenon documents the importance of lipolysis in triglyceride-rich lipoproteins (and the slower rate of nascent HDL particle production) and also highlights the strong negative correlation of triglyceride and HDL cholesterol concentrations.

Ever since, the dynamics of triglyceride-rich lipoprotein clearance have become an important question, particularly with regard to the discussion over optimal metabolic rate testing, a very intensively debated topic among leading individuals in the field (Kolovou *et al.* 2011, Kovář and Zemánková 2015). Unfortunately, still no definitive protocol for a "fat tolerance test" has yet been determined. This is partly due to the problem of fat bolus composition, and principally because of the requirement to continuously follow up triglyceride concentrations for more than 6 hours after fat loading. This is the main limit in applying this type of exact test in the outpatient clinics of preventive cardiology. Recently, more light has been shed on the extent of triglyceride intravasal concentration risk, as presented in three articles of this supplement (Vrablík and Češka 2015, Piťha *et al.* 2015, Vaverková *et al.* 2015).

In addition the direct relationship of remnant particle concentration to pre-clinical parameters of atherosclerosis (Piťha *et al.* 2015) and the combined effect of hypertriglyceridemia on the risk of thrombogenesis and pro-inflammation status (Vaverková *et al.* 2015) are documented in this issue.

During the '80s and '90s, the substantial role played by monocytes/macrophages in atherogenesis was documented. But later, data were presented showing that macrophages in adipose tissue play the predominant role in the development of insulin insufficiency, diabetes, and atherosclerosis. Recent data from experimental models and also tissue culture studies of macrophages document that these changes are due to the important role of adipose tissue in what is known as "sterile infection" or "pro-inflammation status" (Poledne *et al.* 2015), which stimulates atherogenesis and the instability of previously formed atherosclerotic plaque. These experimental data are in concordance with the epidemiological data of Ridker *et al.* (1998), which show higher risk to individuals with slightly increased CRP concentrations within the normal range.

Recent analysis of the atherosclerotic process proposes the direct participation of pro-inflammatory (normally stimulated) macrophages (M1) (Králová *et al.* 2015). On the other hand, alternatively stimulated M2 macrophages are believed to play an anti-inflammatory and atherosclerosis-protective role. Both types of macrophages are present in adipose tissue of experimental animals and their ratio is supposed to be the main determinant of atherogenesis. Unfortunately, only very limited data have been obtained from human adipose tissue. A large transplantation programme operated by the Institute for Clinical and Experimental Medicine has now opened a gateway for the analysis of monocytes/ macrophages in human adipose tissue obtained per-operatively. This new original data are presented in the second part of this supplement (Králová *et al.* 2015, Králová Lesná *et al.* 2015).

The direct influence of macrophages in adipose tissue on the inflammation process in the sub-endothelial space of medium and large arteries is still missing. An indirect effect of molecules produced in adipose tissue on

PHYSIOLOGICAL RESEARCH • ISSN 0862-8408 (print) • ISSN 1802-9973 (online)

Fax +420 241 062 164, e-mail: physres@biomed.cas.cz, www.biomed.cas.cz/physiolres

monocytes located within the arterial wall is supposed. However, there is an opposite alternative which suggests that monocytes/macrophages passing through adipose tissue might change their properties; hence becoming more atherogenic once they leave adipose tissue and then directly invade the arterial wall. This question is still to be clarified.

Rudolf Poledne

References

HAVEL RJ, EDER HA, BRAGDON JH: The distribution and chemical composition of ultracentrifugally separated lipoproteins in human serum. *J Clin Invest* **34**: 1345-1353, 1955.

HOKANSON JE, AUSTIN MA: Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a metaanalysis of population-based prospective studies. *J Cardiovasc Risk* **3**: 213-219, 1996.

KOLOVOU GD, MIKHAILIDIS, DP, KOVAR J, LAIRON D, NORDESTGAARD BG, OOI TCH, PEREZ-MARTINEZ P, BILIANOU H, ANAGNOSTOPOULOU K, PANOTOPOULOS G: Assessment and clinical relevance of non-fasting and postprandial triglycerides: an expert panel statement. *Curr Vasc Pharmacol* **9**: 258-270, 2011.

KOVÁŘ J, ZEMÁNKOVÁ K: Moderate alcohol consumption and triglyceridemia. *Physiol Res* **64** (Suppl 3): S371-S375, 2015.

KRÁLOVÁ A, KRÁLOVÁ LESNÁ I, FRONĚK J, ČEJKOVÁ S, SEKERKOVÁ A, JANOUŠEK L, THIEME F, STŘÍŽ I, ŽDYCHOVÁ J, POLEDNE R: Macrophage phenotypes in the adipose tissue of postmenopausal women. *Physiol Res* **64** (Suppl 3): S427-S433, 2015.

KRALOVA LESNA I, TONAR Z, MALEK I, MALUSKOVA J, NEDOROST L, PIRK J, PITHA J, LANSKA V, POLEDNE R: Is the amount of coronary perivascular fat related to atherosclerosis? *Physiol Res* **64** (Suppl 3): S435-S443, 2015.

PIŤHA J, KOVÁŘ J, BLAHOVÁ T: Fasting and nonfasting triglycerides in cardiovascular and other diseases. *Physiol Res* **64** (Suppl 3): S323-S330, 2015.

POLEDNE R, KRÁLOVÁ LESNÁ I, ČEJKOVÁ S: Adipose tissue and atherosclerosis. *Physiol Res* **64** (Suppl 3): S395-S402, 2015.

RIDKER PM, CUSHMAN M, STAMPFER MJ, TRACY RP, HENNEKENS CH: Plasma concentration of C-reactive protein and risk of developing peripheral vascular disease. *Circulation* **97**: 425-428, 1998.

VAVERKOVÁ H, KARÁSEK D, NOVOTNÝ D, HALENKA M, ORSÁG J, SLAVÍK L: Hypertriglyceridemic waist - a simple clinical tool to detect cardiometabolic risk: comparison with harmonized definition of metabolic syndrome. *Physiol Res* **64** (Suppl 3): S385-S394, 2015.

VRABLÍK M, ČEŠKA R: Treatment of hypertriglyceridemia: a review of current options. *Physiol Res* **64** (Suppl 3): S331-S340, 2015.

ZILVERSMIT DB: Atherogenic nature of triglycerides, postprandial lipidemia, and triglyceride-rich remnant lipoproteins. *Clin Chem* **41**: 153-158, 1995.