

Accumulation of chylomicron remnants and postprandial lipaemia in men with visceral obesity*JCL Mamo¹, GF Watts², H Barrett, D Smith, S Pal and A James*¹Department of Nutrition, Dietetics and Food Sciences, Curtin University of Technology²Department of Medicine, University of Western Australia

Visceral obesity is often the precursor of NIDDM and cardiovascular disease. Increased risk in obesity is attributed to metabolic abnormalities including insulin resistance and dyslipidemia. Unlike non obese subjects cholesterol is not usually elevated in obesity. Rather, there is an accumulation of triglyceride-rich lipoproteins (TRL's). Following secretion, TRL's from the intestine (chylomicrons) and from the liver (VLDL) are hydrolyzed by lipolytic enzymes, before being cleared from blood by receptor pathways. It is presently unclear whether in obesity, a defect in secretion, hydrolysis and/or particle uptake are responsible for hypertriglyceridemia. There is accumulating evidence suggesting that postprandial dyslipidemia is an independent risk factor for cardiovascular disease. However, it is critical to distinguish between the accumulation of large triglyceride rich chylomicrons versus post-hydrolyzed remnant particles. It is the latter which are thought to confer increased risk. What is presently not clear is whether the clearance of the chylomicron remnants is abnormal in subjects with insulin resistance. The hypothesis which formed the basis of this study was that the metabolism of chylomicron remnants is disturbed in viscerally obese non-diabetic subjects and that this is inversely related to the level of insulin sensitivity.

Methods: We recruited 35 male subjects. Exclusion criteria: smoking, diabetes, hypothyroidism, apo E₂/E₂ genotype and the use of lipid lowering or hypertensive agents. Subjects with a total plasma cholesterol greater than 6mM or LDL-cholesterol greater than 4mM were also excluded. Chylomicron metabolism was assessed in response to an oral fat load and was expressed as incremental units of apo B₄₈ and retinyl palmitate (RP). Endogenous and exogenous markers of chylomicrons respectively.

The incremental area under the apo B₄₈ and RP curves following a lipid meal were found to be significantly greater in obese subjects compared to lean controls. We found a significantly higher concentration of plasma apo B₄₈ in obese subjects in the fasted state (37.40 ± 7.8 versus 12.69 ± 1.65 , $p < 0.005$) indicative of an accumulation of remnants. Obese subjects were found to be insulin resistant compared to lean controls, but the level of sensitivity (determined in response to a glucose challenge) did not correlate with the postprandial lipid.

Chylomicron dyslipidemia may be due to overproduction, impaired triglyceride hydrolysis or delayed clearance of remnants post-hydrolysis. The activities of lipoprotein lipase and hepatic lipase were determined in postheparin plasma, however we found no difference between obese versus lean subjects. In contrast, LDL-receptor activity in mononuclear cells was found in obese subjects to be half that of controls (70.9 ± 15.07 versus 38.9 ± 4.6). The LDL-receptor is the primary mechanism by which remnants are cleared in vivo. We have shown that subjects with visceral obesity have an accumulation of small dense postprandial lipoprotein remnants in plasma, which does not appear to be due to delayed conversion of nascent chylomicrons during the post-absorptive state. Rather, subtle and perhaps chronic changes in the clearance of chylomicron remnants might contribute to the elevation of these pro-atherogenic lipoproteins. Insulin, may be central to the metabolic defect of chylomicron remnant dyslipidemia and therefore one would predict that interventions aimed at restoring insulin sensitivity might attenuate the raised concentration of these pro-atherogenic lipoproteins.