European Journal of Clinical Investigation (1993) **23,** 856

Letter to the Editor

CETP-catalysed transfer of cholesterylesters from HDL to apo B-containing lipoproteins in plasma from diabetic patients

Sir,

A recent issue of the EJCI includes a paper entitled *Decreased ability of high density lipoproteins to transfer cholesterol esters in non-insulin-dependent diabetes mellitus* by Ahnadi *et al.* [1].

The idea that some patients with abnormal plasma lipoproteins, including those with non-insulin-dependent diabetes mellitus (NIDDM), have an impaired transfer of cholesterylesters (CE) from HDL to apo B-containing lipoproteins was reported first by Fielding *et al.* [2]. However, other investigators subsequently showed increased transfer rates in dyslipidaemic plasma [3]. In addition, it was found that net mass CE transfer is accelerated in plasma from insulin-dependent diabetes mellitus (IDDM) patients [4]. The plasma activity level of cholesteryl ester transfer protein (CETP) is also increased in complicated IDDM [5].

The work by Ahnadi *et al.* [1] intends to contribute to the solution of the above-mentioned apparent discrepancy by using an *in vitro* CE transfer assay, specifically designed to measure the effects of HDL structure on CE transfer. The authors conclude that patients with NIDDM have an impaired transfer of CE, which is caused partly by a decreased ability of HDL to act as a CE donor.

Although the data are obtained using adequate methodology, it is my opinion that this conclusion cannot be drawn from the present experiments, because the data obtained *in vitro* cannot be extrapolated to the *in vivo* situation. In a way the authors seem to agree with this opinion, as suggested by the last line of their discussion. The reason for the observed low *in vitro* rates of CE transfer, using HDL from NIDDM patients, may very well be that the CE transfer rates are actually elevated in these patients, resulting in low HDL_2 and total HDL-cholesterol, with obvious effects on overall HDL structure. Thus, an accelerated *in vivo* transfer could drain the HDL from part of its CE, making the isolated HDL an inferior CE donor *in vitro*. This possible mechanism has not been recognized by the authors, but may very well explain their results.

It appears that plasma CETP activity levels and the constellation of acceptor lipoproteins are important factors determining the net mass transfer of CE. Active transfer of HDL-CE into the VLDL-LDL pathway may occur in diabetes mellitus, contributing to the tendency for low HDL-cholesterol. Elevated plasma free fatty acids could further accelerate this process [6]. On the contrary, net mass transfer of CE from LDL to HDL may occur in healthy normolipidemic individuals, resulting in high HDL-cholesterol [7].

A. VAN TOL

Department of Biochemistery, Erasmus University Rotterdam, PO Box 1738, 3000 DR, Rotterdam, The Netherlands.

References

1 Ahnadi C-E, Masmoudi T, Berthezène F, Ponsin G. Decreased ability of high density lipoproteins to transfer cholesterol esters in non-insulin-dependent diabetes mellitus. Eur J Clin Invest 1993;23:459–65.

2 Fielding CJ, Reaven GM, Liu G, Fielding PE. Increased free cholesterol in plasma low and very low density lipoproteins in non-insulin-dependent diabetes mellitus: its role in the inhibition of cholesteryl ester transfer. Proc Natl Acad Sci USA 1984;81:2512–16.

3 Tall AR, Granot E, Brocia R, Tabas I, Hesler C, Williams K, Denke M. Accelerated transfer of cholesteryl esters in a dyslipidemic plasma. Role of cholesterol ester transfer protein. J Clin Invest 1987;79:1217–25.

4 Bagdade JD, Ritter MC, Subbaiah, PV. Accelerated cholesteryl esters transfer in patients with insulin-dependent diabetes mellitus. Eur J Clin Invest 1991;21:161–7.

5 Dullaart RPF, Groener JEM, Dikkeschei LD, Erkelens DW, Doorenbos H. Increased cholesteryl ester transfer activity in complicated type I (insulin-dependent) diabetes mellitus. Its relationship with serum lipids. Diabetologia 1989;39:14–19.

6 Lagrost L, Barter PJ. Effects of various non-esterified fatty acids on the transfer of cholesteryl esters from HDL to LDL induced by the cholesteryl ester transfer protein. Biochim Biophys Acta 1991;1085:209–16.

7 Van Tol A, Scheek LM, Groener JEM. Net mass transfer of cholesteryl esters from low density lipoproteins to high density lipoproteins in plasma from normolipidemic subjects. Arteriosclerosis Thromb 1991;11:55–63.