Letters to the Editor

Complement in Type 1 (insulin-dependent) diabetes

Dear Sir,

We read with interest Dr. Charlesworth and colleagues' article about complement in Type 1 (insulin-dependent) diabetes [1]. The authors found low serum levels of the early complement components C1, C3 and C4 in patients with Type 1 diabetes, irrespective of duration of disease and presence of complications. In particular, the reduction in C4 was not related to the possession of null allotypes at C4 gene loci. High fractional catabolic rate values for C3 and C4 were observed in only 2 of 7 patients with recently diagnosed Type 1 diabetes, suggesting that hypercatabolism does not have a major influence in determining the reduction in the circulating levels of such molecules.

Circulating levels of complement result from a balance between synthesis and consumption. Evidence of complement consumption can be unequivocally obtained by the measurement of complement fragments generated during activation [2]. Therefore, in addition to C3 and C4, we measured the activation fragments C3d and C4d in the plasma (collected in EDTA) of 10 patients (5 female, median age 22, range 11–58) with recently diagnosed Type 1 diabetes (duration of disease <3 months) and in 15 healthy subjects (5 female, age 31, 23–40).

C3 and C4 were measured by laser nephelometry using specific antisera (Behring Diagnostics, Hounslow, Middlesex, UK). Results were expressed in g/l. C3d and C4d were similarly assayed after isolation in polyethylene glycol, using anti-C3d (Dakopatts, High Wycombe, Berkshire, UK) and anti-C4 intact (Behring Diagnostics) antisera [3, 4]. Results were expressed as a percentage of a 100% C3d and C4d standard. The fragment-to-parent molecule ratios C3d/C3 and C4d/C4 were derived, in order to obtain indices of complement activation independent of the initial concentration of intact components. These ratios positively correlate with the *in vivo* fractional catabolic rate of C3 and C4 [5, 6]. Differences in mean values between diabetic patients and control subjects were analysed by the Student's *t*-test.

Diabetic patients had values of C3 (mean 0.87 g/l, SD 0.14 g/l) and C4 (0.20 g/l, 0.03 g/l) significantly lower than control subjects (C3: 1.00 g/l, 0.15 g/l, $p < 0.05$; C4: 0.27 g/l, 0.07 g/l, $p < 0.01$), whilst their values of C3d (4.3%, 1.9%), C4d (14.5%, 8.4%), C3d/C3 (5.0, 1.9) and C4d/C4 (75.7, 34.0) did not differ from control subjects (C3d: 4.4%, 1.2%, NS; C4d: 17.6%, 4.4%, NS; C3d/C3: 5.4, 2.6, NS; C4d/C4: 68.6, 25.1, NS). Only one patient had values of C4d and C4d/C4 above the upper limit of normal (mean control val-

ue + 2SD), indicating accelerated catabolism of C4. Another patient had a high value for C3d, but C3d/C3 within the normal range.

These results confirm that low concentrations of C3 and C4 are present in Type 1 diabetes of recent onset. This reduction does not appear to be due to consumption, since indices of complement activation were found to be normal. In agreement with Dr. Charlesworth and colleagues we conclude that the reduction in C3 and C4 is likely to result from impaired synthesis.

Yours sincerely,

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References

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