References

1. Keller U (1986) Diabetic ketoacidosis: current view on pathogenesis and treatment. *Diabetologia* 29: 71–77
2. Thomas TH, Lee MR (1976) The specificity of antisera for the radioimmunoassay of arginine vasopressin in human plasma and urine during water loading. *Clin Sci and Mol Med* 51: 525–536
3. Walsh CH, Baylis PH, Malins JM (1979) Plasma arginine vasopressin in diabetic ketoacidosis. *Diabetologia* 16: 93–96
4. Robertson GL (1977) The regulation of vasopressin function in health and disease. *Recent Prog in Horm Res* 33: 333–385
5. Grant PJ, Tate GM, Davies JA, Williams NS, Prentice CRM (1986) Intra-operative activation of coagulation – a stimulus to thrombosis mediated by vasopressin? *Thromb Haemost* 55 (1): 104–107
6. Rofe AM, Williamson DH (1983) Mechanism for the 'anti-lipolytic' action of vasopressin in the starved rat. *Biochem J* 212: 899–902
7. Spruce BA, McCulloch AJ, Burd J, Orskov H, Heaton A, Baylis PH, Alberti KGMM (1985) The effect of vasopressin infusion on glucose metabolism in man. *Clin Endocrinol* 22, 4: 463–468
8. Rofe AM, Williamson DH (1983) Metabolic effects of vasopressin infusion in the starved rat. *Biochem* 212: 231–239
9. Grant PJ, Davies JA, Tate GM, Boothby M, Prentice (1985) Effects of physiological concentrations of vasopressin on haemostatic function in man. 69: 471–476

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Islet cell antibodies, mumps infection and mumps vaccination

Sir,

In relation to the recent paper by Helmke et al. [1], we would like to communicate our findings on the same subject.

Two hundred and forty-two sera from 184 patients (<20 years of age) with proven mumps infection (immunofluorescence, complement fixation) were collected between 1 and 6 weeks after the first symptoms of disease and their sera tested for the presence of islet cell antibodies (ICA) [2]. The sera were collected in 1984 and 1985 in the cities of Rotterdam and Utrecht, The Netherlands. Most of the patients were hospitalized with complications of mumps, such as meningo-encephalitis, orchitis or pancreatitis. Within this time period the sera of all these patients appeared to be negative for ICA. Only two of them were positive for antibodies against glucagon-producing cells. From 149 other children (aged 16–21 months) sera were obtained before, and 8 weeks and 2.5 years after, mumps vaccination. (The vaccination was carried out in 1981 and 1982 by means of Mumpsxvax, Jeryl Lynn strain, live, Merck, Sharp & Dohme). All those sera were also tested for the presence or absence of ICA. In none of the sera could ICA be detected. None of the vaccinated children developed insulin dependency to date. It should be noted, however, that in this group 2 sera obtained before vaccination and 4 sera obtained 8 weeks after vaccination contained antibodies toward glucagon-producing cells of the islets. Of the 4 positive sera drawn 8 weeks after vaccination, two came from the same children who had already been positive for these antibodies before vaccination. Of the sera obtained 2.5 years after vaccination, no antibodies toward glucagon-producing cells were found. The significance of these findings related to antibodies against glucagon-producing cells, occurring in less than 0.5% of the random population, is unknown [3].

Our findings with regard to the children with mumps infection are at variance with the previous data of Helmke et al. (in 1979–1980, 13 out of 26 ICA positive; in 1980–1981, 7 out of 25 ICA positive) and of Ratzmann et al. (67 out of 86 ICA positive), but agree with the present

results of Helmke et al. (1981–1982, 1 out of 27, in 1982–1984, 0 out of 49 ICA positive) and also with those of Richens & Jones (0 out of 25 ICA positive) [5]. A definite conclusion can be drawn when the international standardization according to the recent Monaco conference is completed [2]. The differences in ICA-positivity in the study of Helmke et al. [1], performed with the same methods and confirmed by retesting, may indeed be due to differences between various mumps-virus strains as shown by the use of monoclonal antibodies [6]. Our findings are not in agreement with explanations which relate an increasing incidence of Type 1 (insulin-dependent) diabetes during recent decennia with mumps infection or vaccination [7], nor do they offer an explanation for the big differences in incidence in western countries [8].

Helmke et al. [1] postulate that mumps vaccination may provoke diabetes, and they suggest that it would be of interest to make a prospective study to find out the incidence of ICA following mumps vaccination [9]. (In their study all the 4 vaccinated children with Type 1 diabetes who were tested had ICA, but a definite causal relationship has not been established; furthermore, the type of vaccine used was not stated in their paper). In none of the sera of the vaccinated children in our prospective study could ICA be detected. All the children were, however, vaccinated with the Jeryl Lynn strain. In view of the foregoing it is conceivable that vaccination with a live attenuated mumps virus other than the Jeryl Lynn strain might yield ICA-positivity more frequently. This implies that, before mass vaccination with any other strain is considered, a study for possible ICA formation would be necessary.

Yours sincerely,
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References

1. Helmke K, Otten A, Willems WR, Brockhaus R, Mueller-Eckhardt G, Stief T, Bertrams J, Wolf H, Federlin K (1986) Islet cell antibodies and the development of diabetes mellitus in relation to mumps infection and mumps vaccination. *Diabetologia* 29: 30–33
2. Marner B, Lernmark A, Nerup J, Molenaar JL, Tuk CV, Bruining GJ (1983) Analysis of islet cell antibodies on frozen sections of human pancreas. *Diabetologia* 25: 93–96
3. Cudworth AF, Botazzo GF, Doniach D (1980) Genetic and immunological factors in type 1 diabetes. In: Irvine J (ed) *The immunology of diabetes*, Edinburgh, pp 67–99
4. Ratzmann KP, Strese J, Witt S, Berling H, Keilacker H, Michaelis D (1984) Mumps infection and insulin-dependent diabetes mellitus (IDDM) *Diabetes Care* 7: 170–73
5. Richens ER, Jones WG (1981) Islet cell antibodies and mumps. *Lancet* i: 507–08 (Letter)
6. Orvell C (1984) The reactions of monoclonal antibodies with structural proteins of mumps virus. *J Immunol* 132: 2622–28
7. North AF, Gorwitz K, Sultz A (1977) A secular increase in the incidence of juvenile diabetes mellitus. *J Pediatr* 91: 706–10
8. Vaandrager GJ, Bruining GJ, Veenhof FJ, Drayer NM (1984) Incidence of childhood diabetes in the Netherlands: a decrease from north to south over North-Western Europe? *Diabetologia* 27: 203–06
9. Otten A, Helmke K, Stief T, Mueller-Eckhardt G, Willems WR, Federlin K (1984) Mumps, mumps vaccination, islet cell antibodies and the first manifestation of diabetes mellitus type 1. *Behring Inst Mitt* 75: 83–88

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