

*The authors reply:*

In their letter Doctors Classen and Classen present their disagreement with our recent current opinion article 'Immunisation and Type 1 Diabetes Mellitus: Is there a link?'<sup>[1]</sup> In contrast to us, they believe that there is clear evidence supporting an association between immunisations and type 1 diabetes mellitus. They refer to their own animal work showing that early immunisations delay the onset of type 1 diabetes mellitus in non-obese diabetic (NOD) mice and to human studies showing an epidemiological association between vaccinations and incidence of type 1 diabetes mellitus.

We agree with Classen and Classen in that various immunisations can modulate the risk of diabetes in NOD mice. However, results obtained from these mouse models should be interpreted with caution and confirmed in human studies because the true relevance of various animal models is not known. For example, a virus (encephalomyocarditisvirus) which lessens the autoimmune process in NOD-mice causes type 1 diabetes mellitus in other mouse strains.<sup>[2]</sup>

We disagree with Classen and Classen in their opinion that human studies have clearly suggested an association between immunisations and type 1 diabetes mellitus. For example, BCG vaccine has been given in Finland to all children at birth since 1941, which according to Classen should be associated with reduced diabetes risk, but the incidence of diabetes in Finland is the highest in the world. It is also higher than in the neighbouring Sweden where BCG has not been given since 1975. Possible effect of *Haemophilus influenzae* type b vaccination has recently been discussed in another forum<sup>[3-5]</sup> and the general view is that this vaccination or its timing has no clear effect on diabetes risk. The possible effect of hepatitis B vaccines still lacks confirmation. We have studied the effect of MMR vaccine in Finland. Although it has been given since 1982 to all children at the age of 14 to 18 months, the incidence of diabetes has so far been increasing linearly even in very young children (<5 years old) indicating no cohort effect

which could be connected to the implementation of the vaccine.<sup>[1]</sup> In addition, we have to be very careful in the interpretation of possible correlations between various vaccines and annual variations in the diabetes incidence rates because they may be biased by several confounding factors.

A large workshop on childhood immunisations and type 1 diabetes mellitus which was organised in Baltimore, US, in 1998 concluded that selective vaccines are protective against diabetes in animals but the data in humans are inconclusive and that no vaccines have been shown to increase the risk of type 1 diabetes mellitus in humans.<sup>[6]</sup> Accordingly, we think that the currently available information does not allow the conclusion that any vaccine is associated with human diabetes. However, further studies are needed to exclude this possibility and carefully designed prospective studies should be considered when vaccination schedules are modified or new vaccines are introduced.

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