A.L. Drash, USA: I said that Dr. Dupre and his group brought us into the ciclosporin age. I think we are in the last stages of the ciclosporin era in terms of its application to diabetes. There is a new very potent immunosuppressive in the field that you need to be informed about, which is called by code FK506. It is a Japanese product (Fujisawa, Osaka), an immunosuppressive agent derived from the fungus of streptomycetes. It is interesting that the Japanese equivalent of the American Food and Drug Administration have refused to allow its use in humans in Japan. However, it is being used in Pittsburgh very actively by Tom Starzl, who is a transplant surgeon. The first scientific report appeared in the New York Times about 2 weeks ago (mid-October 1989) in which the scientific editor reported on 120 cases in which this compound has been used in liver transplantations. The first true scientific report is in the current issue of Lancet [Starzl et al., Lancet 1989;ii:1000-1006], entitled ‘FK506 for Liver, Kidney and Pancreas Transplantations’. Dr. Starzl feels that this is a miracle drug. His hyperbole is that it is 500 times as effective as ciclosporin and has no adverse side effects. We have a great deal of hesitancy in accepting that but we are under considerable pressure to move into clinical trials in newly diagnosed diabetics as Dr. Starzl feels that this compound will have great applications across the world, not only in transplantations but in autoimmune diseases in general. Certainly from the Pittsburgh pediatric perspective, it will not be given to diabetic children until we are fully convinced both of its effectiveness and safety and we are currently doing studies in the BB rat with this compound.

P. Czernichow, France: It is difficult to speak about results that have not yet been completely analyzed and Dr. Bougneres (the leader of the study) would be the best person to answer but as he is not here. I shall give you some information on the preliminary results we have. In June 1988, Dr. Bougneres (Hôpital St-Vincent-de Paul) and Dr. Lévy-Marchal (Hôpital Debré) started a double-blind randomized study involving 60 children. Thirty were given placebo and 30 ciclosporin. The criteria of inclusion were such that we hoped that beta-cell destruction was moderate, like history of poly-uria, moderate loss of weight and blood pH above 7.25. The children received 6 mg/kg of ciclosporin aiming at a blood level of below 50 mg/ml of ciclosporin and with other safety taps which I will not describe. Criteria for total remission were quite severe: no insulin at all, HbA1c below 7%, fasting blood glucose of 140 mg/dl and postprandial blood glucose of < 200 mg/dl. Up to 4 months, the results were identical to what you have seen in the adult studies: 40 % of patients on ciclosporin and 20 % in the placebo group were in total remission. After a year of treatment surprisingly 15 patients in the placebo group and 17 patients on ciclosporin were in total remission. We have learnt from this study the importance of a control group; I also seriously doubt that with the use of a low dose of ciclosporin (6 mg/kg) as we have been using, we are going to get significant results for cure of insulin-dependent diabetes mellitus. J. Dupre, Canada: Do you know about the C-peptide response in these trials? Is there the same dissociation as in the clinical response? P. Czernichow, France: I do not know.
Nerup, Denmark: I think it was clear from Dr. Elias’ presentation that T killer cells are very important in the process leading to diabetes and this is very pertinent knowledge for the last remarks by Dr. Dupre, since the major effect of ciclosporin is to block the transcription of a series of genes in these lymphocytes.