the extraembryonal blood circulation is joined, whereas the embryos retain unrestrained mobility. They come out of parabiosis in a natural way by rejecting the umbilical cords from the extraembryonal circuit at the time of hatching. Despite its profound metabolic influence, the very physiological nature of our method is indicated by the high hatching rate of parabionts, which is 80% with good-quality starting materials (corresponding to the generally observed hatching rate) or even 100% in some experiments.

The described results of vegetative hybridization after parabiosis corroborate our earlier results on the exchange of egg white (Hašek 1952, Hašková 1953, Vojtíšková and Hašek 1953) and indicate that vegetative hybridization can be accomplished in animals, thus enabling better analysis of genetic changes.

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THE 50TH ANNIVERSITY OF TOLERANCE

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The genesis of this special feature was a conversation on tolerance with Juraj Ivanyi, at a function unrelated to science. He mentioned that he was writing a review of Milan Hašek's contribution to the experimental and theoretical development of immunologic tolerance for *Nature Reviews: Immunology* (*1*). This was excellent news, because I had long wondered about Milan Hašek. His contribution to the momentous events of the early 1950s has been debated over the years (see Ivanyi (*1*) and Brent (*2*)), but his key article has remained inaccessible to all but a few scientists, because it was published in Czech (*3*).

Reviews and opinions are valuable, but there is nothing like letting Milan Hašek speak for himself. Juraj indicated he would be willing to translate Hašek's article into English—probably the first time this has formally been done. As a Ph.D. student at Hašek's Institute in the 1960s, Juraj was better placed than anyone to accomplish this task. The editors of *Transplantation*

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were enthusiastic about the idea of publishing Juraj's translation of Hašek (*3*) side-by-side with the Billingham et al. *Nature* article (*4*), and so here we are today.

These two pieces of work arose independently of each other, in a way that is unimaginable in today's communications age and in our infinitely more relaxed political climate. The questions everyone will be asking is, how do they compare? What are their relative merits and contributions?

It is interesting to note the genesis of and the assumptions surrounding each piece of work. It is well known that the foundations for Billingham et al. (*4*) were provided by Ray Owen in 1945 (*5*). Owen demonstrated that cattle twins were hematopoietic chimeras. He correctly deduced that the early exchange of blood cells (the placentae of cattle twins almost invariably share vascular connections) (*6*) resulted in the mutual and lifelong acceptance of the foreign twin's hematopoietic cells. Interestingly, and rather curiously from our modern vantage point, Medawar's group expected that skin grafts between dizygotic cattle twins would be rejected. The motivation for their skin graft studies in cattle twins was the fact that, as Owen had shown, blood grouping was of no value for distinguishing monozygotic and dizygotic twins. Medawar's group did not regard the sharing of hematopoietic systems as sufficient to enable skin graft acceptance—it would be interesting if Leslie Brent could shed some light on this point. They quickly proved themselves wrong. Once it was clear that dizygotic cattle twins were completely tolerant of each other's skin allografts (*7*), the progression to the famous experiment in mice (*4*) was probably clear. It is less clear why the experiments were repeated in chickens, by the injection of 0.2 mL of allogeneic blood intravenously into 11- to 12-day-old chick embryos, demonstrating donor-specific skin allograft tolerance (*4*). Again, Leslie Brent might shed some interesting light on these matters. Could it be that the experiments in chickens were performed first but reported as an addendum to the mouse studies?

The fact that skin allograft rejection was the readout for tolerance probably played a major part in the impact of the article by Billingham et al. (*4*). There had been extensive studies of kidney allograft rejection in dogs by both Dempster (*8*) and Simonsen et al. (*9*), and the extreme vigor of the rejection response had led the authors to question the possibility of the clinical application of transplantation. Out of the blue came perfect transplantation tolerance. The clinical potential, for which surgeons had been striving since the early 1900s (*10*), must have seemed a little closer.

Reading Juraj's fascinating translation, the politics of course stand out as strange to the modern eye. From a biologic standpoint, what stands out is the virtually certain fact that Hašek was unaware of Owen's 1945 article, even though it had been published in *Science* (*5*). Hašek's ingenious system of inducing parabiosis (vascular connections) between embryonic chickens was, in essence, an experimental re-creation in chickens of the synchorial placentae of cattle twins (*6*). Hašek's readout for tolerance was the immunization of the parabionts with each other's washed erythrocytes. His important discovery was the "quite extraordinary"—as Hašek described it—lack of antibody responsiveness to the foreign erythrocytes. Hašek suggested two possible explanations: "the partner's agglutinogens persist in the blood of the second parabiont" or "the partner's agglutinogens' presence during embryonal parabiosis led to their failure to produce antibodies in adult age." Owen had, of course, shown the first of these possibilities to be the case (*5*). In that circumstance, one would not have expected an antibody response to the erythrocytes.

Medawar, although admiring Hašek's work, apparently regarded his 1953 article as simply reproducing Owen's phenomenon in chickens (*1*). That is rather a harsh judgment for an imaginative and powerful experimental system, and for the independent discovery of an important biologic fact, but in terms of scientific precedence and of its impact on tolerance, I think that judgment was right.

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