Adult Mortality After Neonatal Thymectomy in a Marsupial, *Setonix brachyurus* (quokka)[1] (37689)

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Neonatal thymectomy in laboratory mammals causes a severe lymphopenia and a range of immunological defects. The severity of the resultant immunological injury is dependent on the age at which the animal was thymectomized (1), the maximum effect being achieved by thymectomy within 24 hr of birth. Thymectomy after this time has a less marked effect; however, mice thymectomized in adult life have been shown to have a markedly reduced lifespan (2).

The reduced lifespan of neonatally thymectomized laboratory mammals can be attributed to the occurrence in many mouse strains (3) and in some other species (4–6) of a "postthymectomy wasting" or "runting" syndrome. No information has come to hand on the natural lifespan of those animals which do not runt after neonatal thymectomy.

The quokka (*Setonix brachyurus*, Quoy and Gaimard) is a small herbivorous marsupial unique to Western Australia. The adults weigh about 3.5 kg. The young are born after a 28-day gestation period and spend 180 days in the pouch. Animals become sexually mature before 400 days in captivity, but only reach adult dentition at about 700 days (7). In common with other members of the family Macropodidae, the quokka has two pairs of thymus glands (8), one pair in the usual position in the chest and the other, larger, pair situated subcutaneously just above the clavicle.

Neonatal thymectomy in the quokka causes a long-lasting lymphopenia; however, it does not cause growth defects or any form of wasting disease (9), and at one year, intact and thymectomized animals are indistinguishable morphologically. The antibody response is impaired throughout pouch life, but returns to normal once the animals become independent of the mother (10).

Phytohaemagglutinin (PHA) is believed to specifically stimulate thymus-dependent lymphocytes in culture, and thus provide an indirect measure of cellular immune competence (11, 12). Leucocytes from neonatally thymectomized pouch young have a markedly reduced response to stimulation with PHA *in vitro*, but this response also increases after the end of pouch life, although it does not reach normal levels (13, 14).

Materials and Methods. A group of 10 quokkas were thymectomized as described previously (9). The superficial thymus was removed before 10 days postpartum and the thoracic thymus before 20 days. The animals were housed in individual pens of 50 ft^2 and fed *ad libitum* on specially prepared nuts or on enriched chaff (15). All animals had free access to water. A control group of 19 animals were kept under similar conditions.

Results. Mortality curves for the two groups of animals are shown in Fig. 1. A probit analysis of the mortality curve for thymectomized animals gave a mean lifespan of 78 weeks. A comparison with the control group at this time showed that the difference in mortality was just not significant ($0.05 < p < 0.1$). A further comparison at 156 weeks was highly significant ($p < 0.01$).

Only two animals have been available for detailed pathology, because animals do not

[1] This work was supported by the Australian Research Grants Committee, the University of Western Australia Research Grants Committee, and by a grant from C. S. I. R. O. to H. Waring for marsupial research.

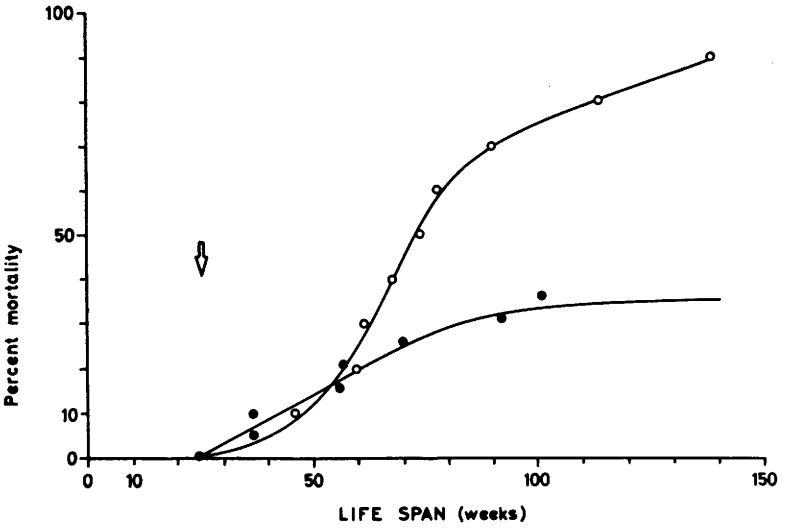

FIG. 1. Percentage mortality of neonatally thymectomized quokkas (open circles) compared to intact controls (closed circles). The arrow indicates the end of pouch life.

survive well in cages, and under yard conditions, dead animals are not immediately detected. One had a massive infection with the yeast *Cryptococcus neoformans*. The second animal had no symptoms detectable by histopathology.

Discussion. Thymectomized quokkas do die throughout pouch life; however, there is no differential mortality compared to intact controls during this period (9). The normal lifespan is more than 10 years, (7) and, hence, the mean age at death of 1.5 years for thymectomized animals represents a very considerable reduction.

The preponderance of deaths in wild animals in the field is during the hot dry summer, when the animals are about 1 year old (16), and our results for yard animals are consistent with this pattern. The majority of thymectomized animals die at 1–1.5 years of age, but the peak is in the cold wet winter. This suggests that death may be associated with cold stress in these animals.

Jeejeebhoy (2) has shown that the majority of mice dying after thymectomy in adult life had no detectable symptoms at autopsy, and our results, though meager, are consistent with his findings.

Two interpretations of the differential mortality in adult life present themselves for consideration. (i) A small population of thymus-processed cells is released before thymectomy. This population is sequestered in the peripheral lymphoid tissue, protected by the passive transfer of antibody from the mother. When this ceases, shortly after the end of pouch life (17), the population of immunocompetent cells is gradually used up, and when it declines below a threshold level, the animal dies. (ii) Alternatively, the thymus may have some as yet undiscovered direct relationship to longevity, perhaps associated with general metabolism or cell replication.

We have no information as yet which would enable us to distinguish between these hypotheses.

Summary. The lifespan of the quokka, a small marsupial, was shown to be markedly reduced after neonatal thymectomy, but this was not associated with the development of a wasting syndrome. The normal lifespan of intact animals is more than 10 years; however, most neonatally thymectomized quokkas died before 3 years.

We thank Messrs. W. Evans, L. Smallacombe, G. Benwell, W. Bartholomaeus, and M. Price for animal husbandry, and Mr. N. A. Campbell for statistical advice.

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Received July 30, 1973. P.S.E.B.M., 1973, Vol. 144.