

POSTNATAL PHYSICAL DEVELOPMENT IN JUVENILE NEW ZEALAND WHITE RABBITS

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Over the past 10 years, the safety of pharmaceuticals, but also of food ingredients and chemicals, in neonates and juveniles has become an issue of special interest. Both the FDA and EMEA developed special guidelines to evaluate the safety of pediatric pharmaceuticals in juvenile animals. In these guidelines, a case-by-case approach is indicated for study designs and species to be used. In this kind of studies, physical postnatal development is routinely tested in rodents (rats and mice). For scientific and/or practical reasons however, other species may also be used.

In prenatal developmental toxicity studies, the rabbit is frequently used as the second species of choice. As a consequence, as for rats and mice, there are a lot of data available about the (toxic effects on) prenatal development of rabbits. In contrast, hardly any information is available about postnatal development of rabbits. In this pilot study, we examined pup survival, growth and sexual- and physical development in control non-treated New Zealand White rabbits.

MATERIALS AND METHODS

Pregnant New Zealand White rabbits were obtained from Centre Lagos, France. Rabbits were housed under standard conditions in cages with Noryl nesting boxes (bottom area 1300 cm², Tecnilab, the Netherlands). Extra straw and hay was added to the cages to build a nest. During gestation and lactation body weights of dams and pups were recorded regularly. After birth, pups were individually marked and examined for developmental parameters (see Table 1). On PN day 28, day of weaning, pups and dams were sacrificed (Euthasate®).

RESULTS

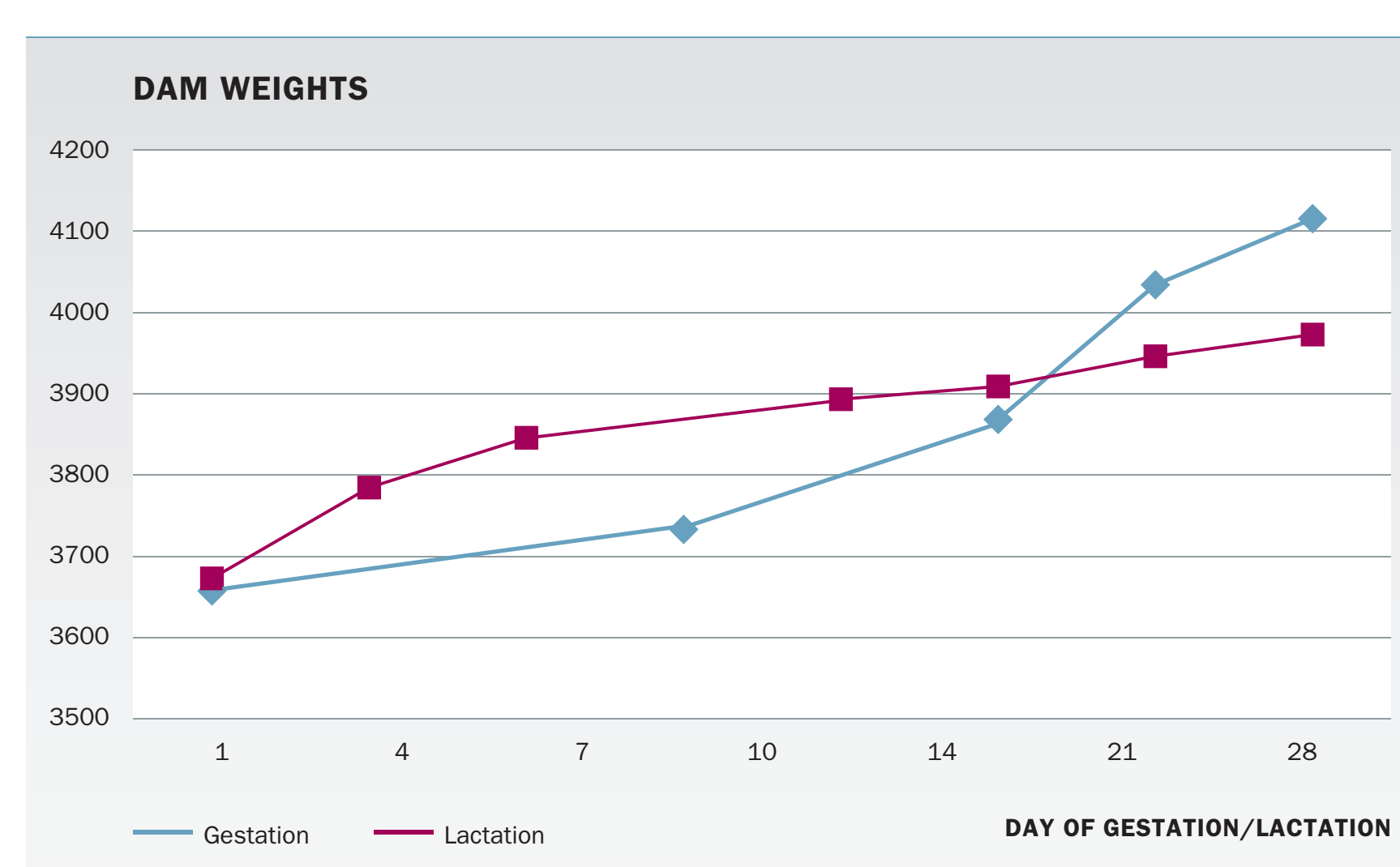


Figure 1: Body weights of dams during gestation and lactation. At daily observations all dams were sparsely haired. The hair was used to build a nest.

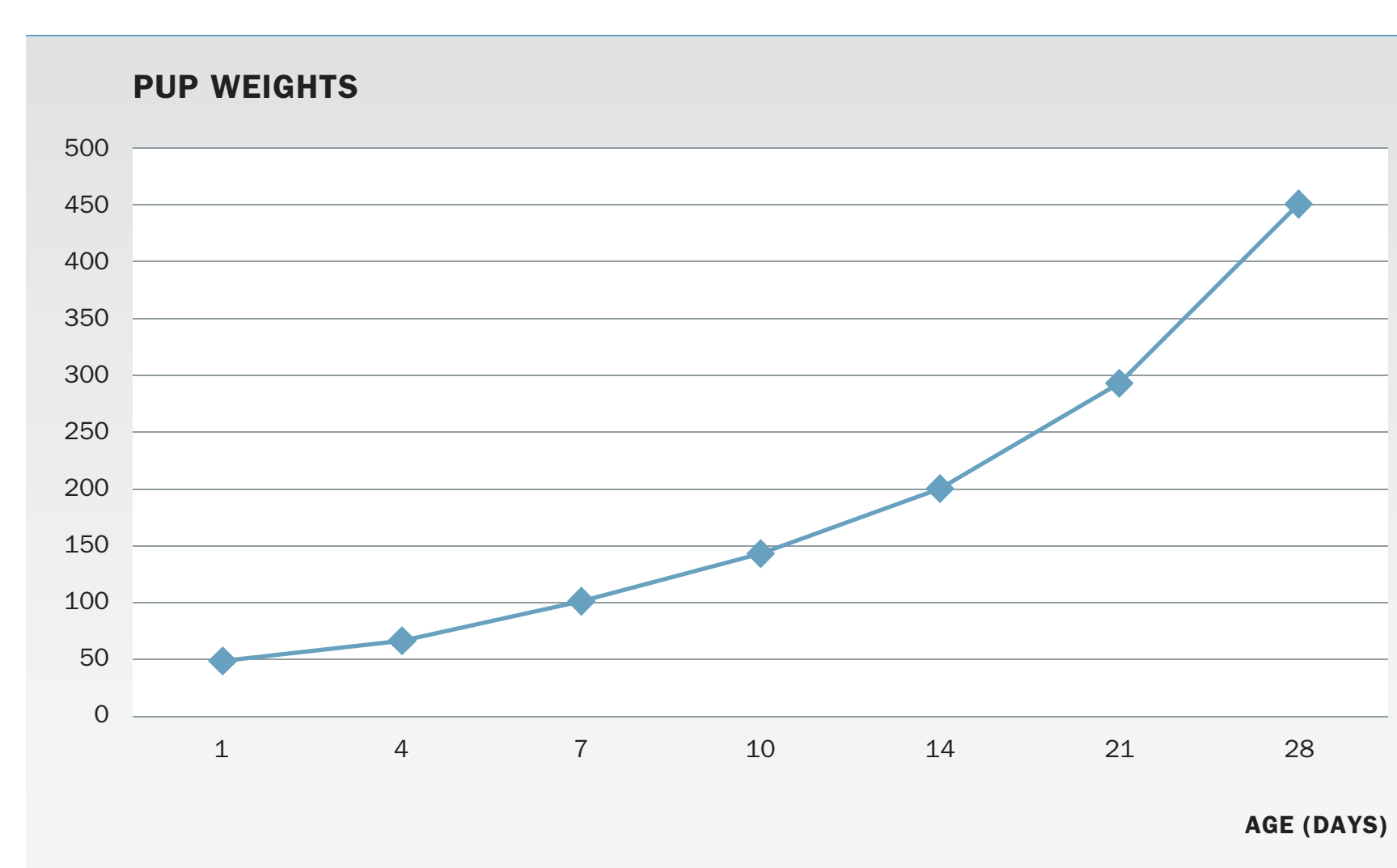


Figure 2: Pup weights. Mean birth weight was 50 g and mean pup weight at weaning was 450 g.

External examination	Surface righting
Weights	Body elevation
Survival	Last day of dragging
Sex / anogenital distance*	Last day of circling
Eye opening	Head elevation for > 1 minute
Hair growth	Hopping

Table 1: Physical developmental landmarks examined in rabbit pups during the lactation period. *: The sex of male and female pups was difficult to discriminate, both by visual examination and by measuring anogenital distance (mean distance for males was 4.2 and for females 3.8 on PN 28). If sex of pups is of vital importance, sex determination in rabbits should be determined by hormonal analysis.

Reproductive data	Descriptor
Females mated/pregnant	10/10
Mating index	100%
Female fecundity index	100%
Female fertility index	100%
Gestation index	100%
Duration of gestation	30.1 days
Females with liveborn pups	10
Females with stillborn pups	1
Female with all stillborn pups	0

Table 2: Reproductive data

Pup survival data	Descriptor
Pups delivered (mean number of pups per litter)	93 (9.3)
Liveborn pups (live birth index)	92 (99%)
Stillborn (mortality day 1)	1 (1.1%)
Pups lost:	
PN day 1-4	11*
PN day 5-7	10*
PN day 8-10	2
PN day 11-14	5
PN day 15-21	1
PN day 22-28	0
Viability index PN 1-28	69%

Table 3: Pup survival data. *: The number of pups lost between PN days 1-7 was relatively high because two dams delivered outside the nesting box. Most of these pups did not survive indicating the importance of nesting boxes for breeding rabbits.

Physical developmental landmarks	Range of days the pups were found positive
Eye opening	PN day 4-10
Hair growth	PN day 1-3
Surface righting	PN day 1-5
Body elevation	PN day 4-10
Last day of dragging	PN day 7-10
Last day of circling	PN day 4-14
Head elevation for > 1 minute	PN day 7-14
Hopping	PN day 14-21

Table 4: Physical developmental landmarks

CONCLUSION

As rodents, rabbits can also be used to study post-natal physical development, e.g. as part of a combined pre- and postnatal developmental toxicity study. The use of nesting boxes is recommended. Sex determination in juvenile rabbits should be supported by hormonal analyses.