Harmonisation of weaning policy for macaques used in research and testing

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NC3Rs
National Centre for the Replacement, Refinement and Reduction of Animals in Research

Presentation plan

- Background to the issue and PSGB report
- Natural weaning
- Variation in weaning policy
- Reasons for artificial weaning
- Effects of artificial weaning
- Conclusions
- Moving forward - Centre for Macaques

Background - Macaques used in research and testing world-wide

Rhesus *M. mulatta*

Stump-tailed *M. arctoides*

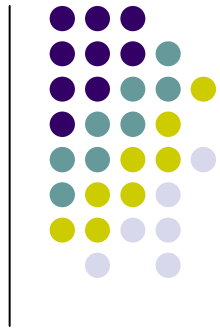
Bonnet *M. radiata*

Pig-tailed *M. nemestrina*

Long-tailed/Cynomolgus
M. fascicularis

Japanese
M. fuscata

Appendix A to the Council of Europe Convention ETS 123

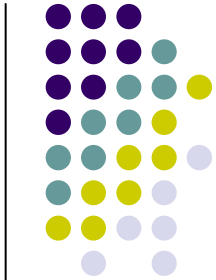


- Provides guidelines for the accommodation and care of animals used in scientific procedures
- Revised text has just been adopted (15 June 2006)
- Primate Expert Group was asked to consider the age at which macaques should be weaned
- PSGB Captive Care Working Party decided to explore this question in greater detail
- A reasoned consideration of weaning policy is important for good animal welfare and good science (which depends on healthy, well-adjusted animals)

Natural weaning

- Takes place in the wild and in some laboratory colonies
- Occurs around 12-14 months of age (Southwick et al. 1965, Lindburg 1971, Harvey et al. 1987)
- Mother gradually discourages infant from suckling
- Infant remains close to mother for comfort and social support
- Interactions with peers increase around 12 months of age
- Natural group composition enables learning of skills for survival and reproduction

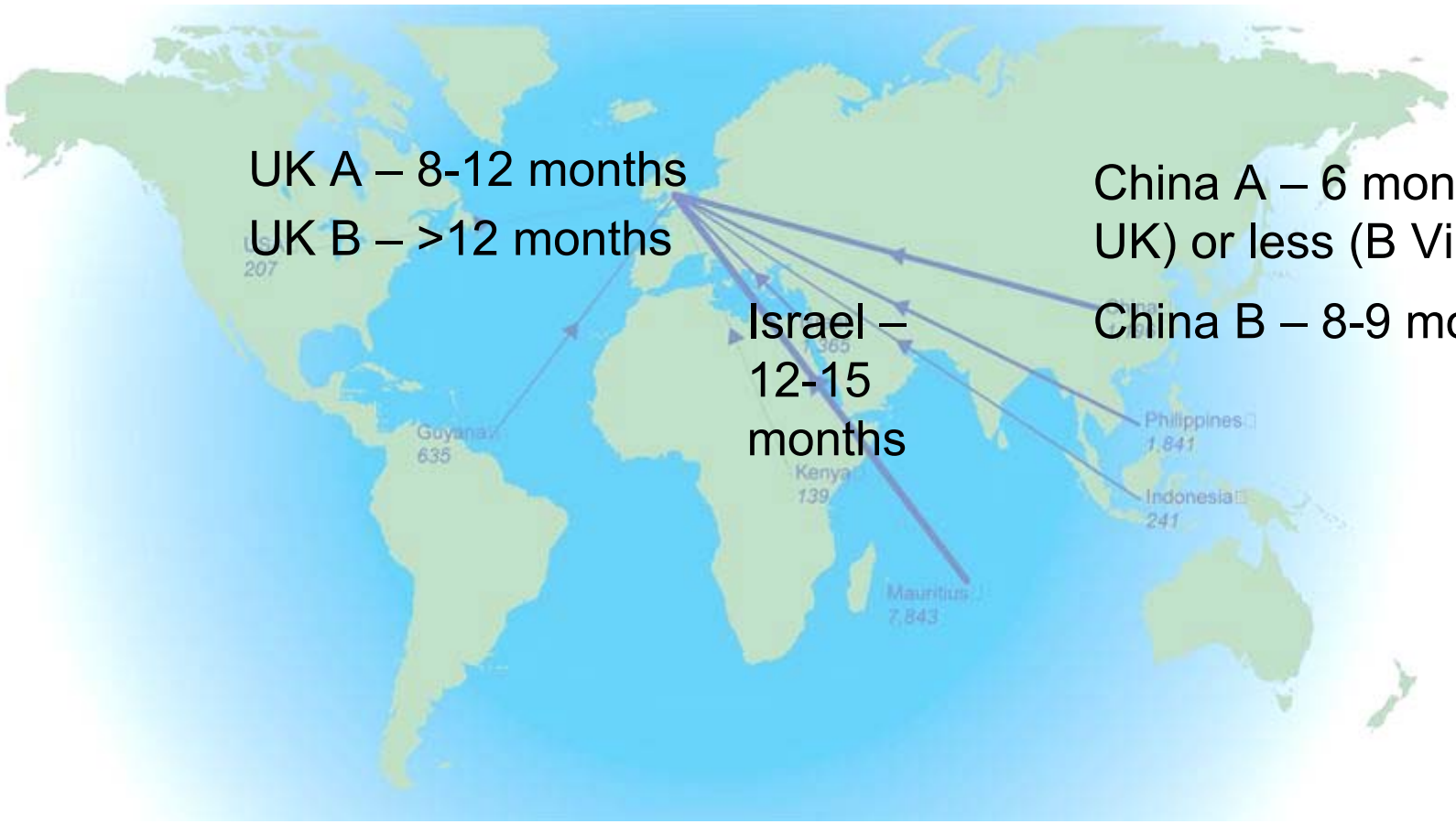
Minimum and preferred weaning ages for macaques specified in guidelines on laboratory primate husbandry and care



Guideline	Minimum (months)	Preferred (months)
IPS Guidelines 1993, 2006	12-18	-
Berlin Workshop (Poole et al. 1994)	6	10-12
Home Office (Code of Practice Breeding) 1995	6 (1kg)	12
PVEN (Poole & Thomas 1995)	6	12
Council of Europe Primate Expert Group 2003	8	12
EC SCAHAW 2002	10-12	-
LASA/MRC 2004	12	-

Conforming to these is no guarantee for producing healthy, well-adjusted animals. Trend over time towards later minimum weaning age.

World-wide variation



There is also variation between breeding centres within and between countries

Reasons for artificial weaning

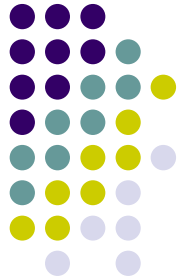
Separating the infant from its mother prior to the natural (biologically normal) age of weaning

- Maximising reproductive output – e.g. weaning at 6 months of age (when infants can survive without the mother) reduces lactational amenorrhoea and can advance next conception (e.g. Kotera et al. 1975, Goo & Fulgate 1984, but see Wallis & Valentine 2001 for *Papio*)
- Minimising contamination with disease – e.g. artificial weaning to peer groups or single housing to prevent B-virus infection (e.g. Zwartouw et al. 1984, Welshman 1999)
- Needs of the experimental protocol – e.g. models of stress, depression, immune deficiency
- Maternal rejection, mis-mothering or illness

Caveat

- Large literature on maternal separation early in life, but very few studies which systematically compare effects of different weaning ages and rearing environments under controlled husbandry and management conditions

Short-term effects of separation from the mother

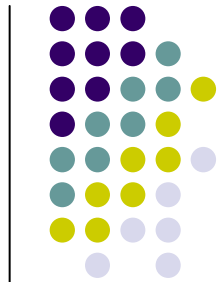


- Behavioural changes –
  - agitation/protest phase – increased locomotion, distress vocalisations and oral and ingestive behaviours
  - depressive/despair phase – slouched (foetal-like) withdrawn postures, reduced motor activity, decreased play, increased self-mouthing and self-clasping, failure to eat
- Influenced by age at separation, familiarity with the environment, presence or absence of allo-parenting figures, and species (Laudenslager & Boccia 1996)

- Immunological effects (Coe 1993, Capitanio 1998) – e.g. decreased capacity to mount an antibody challenge to antigenic challenge – are correlated with behavioural changes (Laudenslager et al. 1990)
- Can be buffered by a familiar environment and companion (Laudenslager & Boccia 1996)

- Also disturbances to HR, T, EEG and sleep (Reite 1981, Sackett & Terao 1992)

Effects on social and sexual behaviour



- Absence of psychologically secure base impedes exploratory behaviour, which can in turn impede social skills –
  - Peer-reared animals show less sexual and play behaviour and more aggression than mother-reared animals (e.g. Ruppenthal et al. 1976, Platt et al. 1996)
  - Nursery-rearing associated with increased incidence of neophobia which persists into adulthood (Timmermans 1997)
  - Mother-reared animals outrank peer-reared and surrogate-peer-reared animals in adulthood (Bastian et al. 2001)
- Socialisation with conspecifics and humans may counter some of these effects for nursery-reared animals (Sackett et al. 2002)

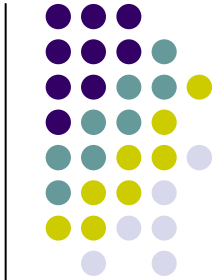
Effects on maternal behaviour

- Peer-rearing can lead to poor reproductive performance and maternal behaviour (e.g. Goldfoot 1977, but see Timmermans & Vosen 1996)
- Hand-rearing has a negative effect on adult maternal behaviour (e.g. Harlow et al. 1971, Ruppenthal et al. 1976)
- Presence of mother in the wild is associated with improved reproductive success (Macdonald Pavelka et al. 2002)

Effects on abnormal behaviour

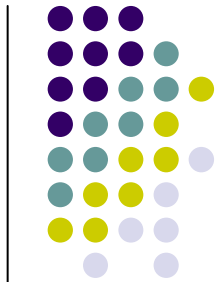
- Artificial weaning and nursery rearing are associated with various abnormal behaviours in juveniles and adults, e.g. - self-injurious behaviour, self-clasping, bizarre postures, rocking, regurgitation with reingestion
  (e.g. Capitanio 1986, Goosen 1989, Platt et al. 1996, Kraemer 1997, Bellanca & Crockett 2002)

Effects on growth and weight



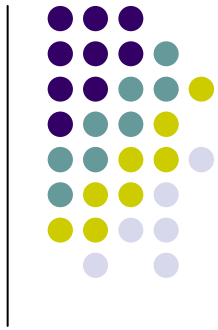
- Animals weaned at 6 or 8 months of age were found to be lighter at 12 months than infants left with their mothers until that time, but survival to 2 years was unaffected (Goo & Fulgate 1984)
- Weaning of light as opposed to heavy animals is associated with increased risk of post-weaning chronic diarrhoea (Munoz-Zanzi et al. 1999)
- Artificial weaning has also been correlated with diarrhoea, which can lead to weight loss (SICONBREC 1995)

Effects on immune competence



- Artificial weaning and separation experiences can have immunosuppressive effects which can compromise physical health (e.g. Reite 1987, Laudenslager 1988)
- Separation experiences early in life are associated with deficient immune responses in adulthood (Reite 1987, Laudenslager et al. 1985, Coe 1993)
- Normal maternal care may be important for the development and maintenance of the physiological set points for certain immune responses (Laudenslager et al. 1990, Gordon et al. 1992)

Species and individual differences



- Changes in behaviour following maternal separation are species dependent – *M. nemestrina* show less allo-maternal care than *M. radiata*, so the agitation phase progresses to the depressive phase in *M. nemestrina* (Laudenslager et al. 1990)

- "High reactive" individuals (15-20% of captive and wild populations) (Suomi 1999)
  - leave their mothers later
  - explore their environment less
  - tend to be shy with peers
  - are more likely to exhibit depressive-like reactions to short-term separations
  - show greater physiological change and immunosuppression

Outcome

- Artificial weaning can have implications for animal welfare, management of social groups, colony productivity and scientific data
- Use of macaques as models of normal humans depends on physically and behaviourally healthy animals able to cope with the laboratory environment (Poole 1997, Reinhardt 2002, 2004, Russell 2002, SCAHAW 2002, Schapiro 2000)

Conclusions

- Colony managers should seek to produce animals that are physically and behaviourally healthy (for good animal welfare and good science) – weaning ≥12 months of age from a species-normal social grouping is optimal
- Attention should be paid to the species and individual – monitor independence from the mother, check body weight, batch wean with compatible peers
- Management practices and breeding systems should be designed to produce behaviourally competent future breeders and avoid hand-rearing – wean ≥18 months of age
- Hand-reared animals should not be used as future breeding stock and may be inappropriate for some research purposes – inform users which animals are hand-reared/mother-reared

Moving forward – Centre for Macaques (CFM)

- Provides secure supply for UK academic use – largely neurosciences
- Aims to be centre of excellence in primate welfare and care and to avoid importation
- Breeding groups comprise 1 male and up to 12 females plus offspring
- Large, enriched indoor enclosures
- High health status, B virus free

CFM weaning policy

- Age – ≥ 12 months of age
- Weight – ≥1.5kg
- Behaviour – independence from mother
- Half-siblings weaned together
- Housed in mix-sex groups until issue (18-24 months of age)
- Hand-reared animals are integrated with peers as early as possible
- Socialisation with humans (around routine husbandry and feeding and during dedicated socialisation period)

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- Feedback to **mark.prescott@nc3rs.org.uk**