Rabies in wild dogs

SIR — The African wild dog *Lycaon pictus*, probably the most endangered large carnivore in Africa[1], has been the subject of conservation research since 1985 in Serengeti National Park and Ngorongoro Conservation Area in Tanzania, and since 1987 in the Masai Mara region of Kenya. In 1989, a Kenyan pack which died from rabies[2], a disease not previously confirmed in wild dogs, included some handled by researchers for radio collaring[3] and vaccination against rabies. Between 1985 and 1990 in the two conservation areas, four of eight unvaccinated study packs (a total of 58 dogs) died 2–5 months after radio collaring, with rabies confirmed in one pack in 1990 (ref. 4).

Following these losses, an attempt was made to vaccinate the remaining study packs in both countries using an inactivated vaccine delivered by air-pressurized darts. All study packs (n=7) died or disappeared within a year of vaccination. Although no known outbreak of rabies occurred in other wildlife, and tissue samples were not available in the conservation areas, rabies was again suspected. However, packs not vaccinated and without radio collars still existed in or near the study areas.

Serum samples taken up to 2 years before vaccination showed that packs had been exposed to rabies with some individuals carrying significant, possibly protective levels of rabies-neutralizing antibody[4]. This begs the question "why vaccinate?"

The feature common to all packs was 'handling'. Many mammalian species carry latent viruses, including rabies[5], which can be reactivated by stress in some cases. Handling-induced stress, as measured by highly elevated peripheral serum cortisol concentrations, results from immobilization of captive wild dogs[6]. Corticosteroids tend to inhibit the body defences, which prevent latent infections from becoming apparent[7]. This stress mechanism perhaps reactivates rabies virus latent in 'handled' carrier dogs with the disease spreading within, but not between, the widely separated packs, by oral social contact. Losses of all packs after vaccination, together with sporadic pack deaths after collaring, could be explained by this hypothesis, as any carrier dog(s) would be 'hit' during whole pack vaccination but only selected by chance for radio collaring.

It is possible that rabies virus persists in wild dogs in a normal host–parasite relationship[5,8] with some naturally immune individuals. This stable system could be disrupted by handling-induced stress in some individuals, resulting in early death[9] of dogs in packs, and vaccine-induced delay[10] in emergence of rabies in the vaccinated packs.

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1. Ginsberg, J. R. & Macdonald, D. W. *IUCN*, World Conservation Union, Gland, Switzerland (1990).
2. Scott, J. *Painted Wolves* (Hamish Hamilton, London, 1991).
3. Fuller, T. K. & Kat, P. W. *Afr. J. Ecol.* **28**, 330–350 (1990).
4. Gascoyne, S. C. *et al. J. wildl. Dis.* (in the press).
5. Carey, A. B. & McLean, R. G. *J. appl. Ecol.* **20**, 777–800 (1983).
6. van Heerden, J. & Kuhn, F. *S. Afr. J. wildl. Res.* **15**, 80–84 (1985).
7. Kaplan, C. (ed.) in *Rabies The Facts* 1–21 (Oxford University Press, 1977).
8. May, R. M. *Nature* **320**, 13–14 (1986).
9. Soave, O. A. *Am. J. Vet. Res.* **25**, 268–269 (1964).
10. Haig, D. A. in *Rabies The Facts* (ed. Kaplan, C.) 53–69 (Oxford University Press, 1977).

Origin of rodents and guinea-pigs

SIR — Our maximum parsimony (MP) analysis[1] of protein sequence data suggested that the order Rodentia may not be monophyletic but that the guinea-pig-like rodents (Caviomorpha) may have branched off earlier than the separation of the rat-like rodents (Myomorpha) from the primates. Our hypothesis, represented as ((Myomorpha, Primates), Caviomorpha), will be called tree III; the traditional view ((Myomorpha, Caviomorpha), Primates), tree I; and the third alternative ((Caviomorpha, Primates), Myomorpha), tree II. But in a maximum likelihood (ML) analysis of a similar set of protein sequences Hasegawa *et al.*[2] did not find significant preference for tree III. Arguing that the ML method withstands the effect of unequal evolutionary rates among lineages, they concluded that our study may represent an example of the unequal rate effect on parsimony analysis. We would like to make three comments.

First, the ML method is model-dependent. For example, for α-crystallin A, the difference in ML value between trees I and II is only 0.4 for the Dayhoff model of amino-acid substitution, but 6.3 and 5.9 for the proportional and Poisson models, respectively[2].

Second, for the ten proteins used, the ML method supports tree I for three proteins, tree II for four proteins, and tree III for three proteins, if the Dayhoff model is used[2]. This means that for most of the proteins the ML method fails to identify the true tree, regardless of which of the three trees is the real one. The same conclusion holds for the other two models of amino-acid substitution. This fact contradicts the claim[2] that the ML method is robust against the effect of unequal rates.

Third, the unequal rate effect is stronger for divergent sequences than for well conserved ones. The table shows the degree of divergence from the outgroup sequence to the human, myomorph and guinea-pig sequences for each protein. As β-globin has an evolutionary rate close to the mean rate for mammalian proteins[3], it may be used as a reference. Let us therefore take α-crystallin A, α-globin, β-globin, lipoprotein lipase and lipocortin as conservative proteins (group I), because their degree of divergence from the outgroup sequence is smaller than or close to that for β-globin. For all these proteins the ML and MP methods are congruent, and both support tree III, except for α-crystallin A (ref. 2). In contrast, for the other five proteins in the table, which may be considered as nonconservative (group II), the ML and MP methods often do not support tree III; when all the proteins in group II are considered together, the ML method supports tree I, whereas the MP method supports tree II. Thus, if tree I is indeed the true tree, then the

Proportion of amino-acid differences between an outgroup (OU) and a human (HU), myomorph (MY) or guinea-pig (GP) sequence

Protein	OU–HU	OU–MY	OU–GP
Outgroup: marsupial			
α-crystallin A	0.10	0.09	0.09
α-globin	0.19	0.23	0.25
β-globin	0.26	0.31	0.30
α-lactalbumin	0.46	0.55	0.55
pancreatic ribonuclease	0.34	0.34	0.38
Outgroup: bird			
lipoprotein lipase	0.23	0.23	0.27
lipocortin	0.28	0.32	0.28
insulin	0.38	0.41	0.51
nerve growth factor-β	0.42	0.47	0.43
Outgroup: factor X			
factor IX	0.63	0.61	0.63

ML method supports the true tree only for the group of nonconservative proteins but not for the group of conservative proteins. This would not be a good property. It is more reasonable to argue that tree III is the true tree and the ML method supports this tree for the group of conservative proteins.

In conclusion, there is actually no conflict between the result of Hasegawa *et al.* and ours, because when the more divergent sequences are excluded their analysis also supports our hypothesis. But as we have noted[1], more sequence data are required to resolve whether rodents are polyphyletic or whether our analysis represents a dramatic example that unequal rates of evolution can consistently mislead parsimony inference.

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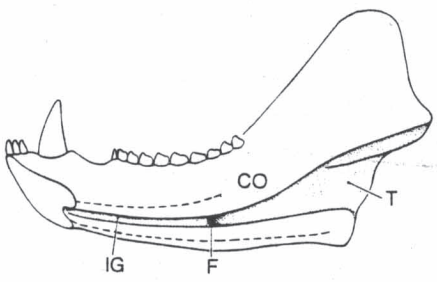
1. Graur, D., Hide, W. A. & Li, W.-H. *Nature* **351**, 649–652 (1991).
2. Hasegawa, M., Cao, Y., Adachi, J. & Yano, T.-A. *Nature* **355**, 595 (1992).
3. Li, W.-H. & Graur, D. *Fundamentals of Molecular Evolution* (Sinauer, Sunderland, Massachusetts, 1991).

No Palaeocene 'mammal-like reptile'

SIR — Fox *et al.*[1] believe that a tooth-bearing fragment of a dentary and four isolated teeth of a distinctive new taxon, *Chronoperates paradoxus*, from the Palaeocene of Alberta, Canada, extend the record of 'mammal-like reptiles' (or, properly speaking, nonmammalian synapsids) by some 100 million years. A review of the anatomical evidence at hand does not bear out their remarkable claim.

Fox *et al.* enumerate four features in support of their interpretation of *Chronoperates* as a nonmammalian cynodont: (1) single-rooted lower postcanines with transversely narrow, multiple-cusped crowns lacking cingula; (2) presence of pseudoprismatic enamel; (3) retention of postdentary bones including a splenial; (4) small masseteric fossa.

First, it should be pointed out that the postcanine teeth are, in fact, quite distinct from those of derived Triassic nonmammalian cynodonts such as *Microconodon* mentioned by Fox *et al.* In *Microconodon*[2,3] and the closely related *Pseudotriconodon*[4], the multiple-cusped postcanines typically have at least incipiently divided roots. Furthermore, these teeth have anteroposteriorly aligned, rather than obtusely angled, cusps, and lack the peculiar interlocking of crowns found in *Chronoperates* (and similarly in various mammalian taxa). The derived absence of cingula is a character of doubtful phylogenetic significance[4]; cingula are also absent or at best slightly developed in the early Jurassic *Sinoconodon*, which is considered the most primitive known mammal by many authors[5,6].



Dentary of the derived nonmammalian cynodont *Diademodon* (based on ref. 12) in lingual view to show the trough for the postdentary bones (T), posterior foramen for the mandibular canal (F) and articular facets ('scars') for the splenial (broken lines) and coronoid (CO). Note forward continuation of the trough as internal groove (IG).

Second, the phylogenetic significance of pseudoprismatic ultrastructure of the enamel has been the subject of continuing debate. Recent work indicates that most Mesozoic mammals (or mammaliaforms) have pseudoprismatic or 'preprismatic' enamel[7].

Third, the alleged 'posteromedial trough' is rather different from the trough for the postdentary bones (articular, prearticular, surangular, angular) on the dentaries of nonmammalian cynodonts (see figure) and primitive mammals and is more likely to represent the posterior entrance of the mandibular canal. Significantly, *Chronoperates* lacks the internal mandibular groove for the more anterior portion of Meckel's cartilage (the posterior portion being represented by the articular bone) found in nonmammalian cynodonts and primitive mammals[8]. The 'scar for splenial and prearticular' is quite unlike the corresponding features on the lingual surface of the dentaries of nonmammalian cynodonts (see figure). There is no feature on any known dentaries of undoubted nonmammalian cynodonts that can be homologized with the 'hook-shaped depression' (which might be a preservational artefact).

Finally, the full extent of the masseteric fossa cannot be determined on the holotype of *C. paradoxus* owing to the fragmentary condition of the coronoid process, but the masseteric fossa in all advanced nonmammalian cynodonts is as extensive as in mammals[9].

The fossils currently available do not justify classification of *Chronoperates* as a nonmammalian cynodont and the resultant range extension of about 100 million years for nonmammalian synapsids. *Chronoperates* shares no clearly derived characters with any known taxon of nonmammalian cynodonts[5,10], and Novacek[11] noted that the dental differences between this form and symmetrodont mammals are rather subtle. There is a clear need for more complete cranial material to determine the precise affinities of this interesting new taxon.

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1. Fox, R. C., Youzwyshyn, G. P. & Krause, D. W. *Nature* **358**, 233–235 (1992).
2. Simpson, G. G. *Am. J. Sci.* **12**, 87–108 (1926).
3. Sues, H.-D., Olsen, P. E. & Kroehler, P. A. in *In the Shadow of the Dinosaurs: Early Mesozoic Tetrapods* (eds Fraser, N. C. & Sues, H.-D.) (Columbia University Press, New York, in the press).
4. Hahn, G., Lepage, J. C. & Wouters, G. *Bull. Soc. belge Géol.* **93**, 357–373 (1984).
5. Hopson, J. A. in *Origins of the Higher Groups of Tetrapods* (eds Schultze, H.-P. & Trueb, L.) (Cornell University Press, Ithaca, 1991).
6. Luo, Z. & Crompton, A. W. in *Mammal Phylogeny* Vol. 1 (eds Szalay, F. S., Novacek, M. J. & McKenna, M. C.) (Karger, Zürich, in the press).
7. Carlson, S. J. in *Skeletal Biomineralization: Patterns, Processes and Evolutionary Trends* Vol. 1 (ed. Carter, J. G.) 531–556 (Van Nostrand Reinhold, New York, 1990).
8. Krebs, B. in *Early Mammals* (eds Kermack, D. M. & Kermack, K. A.) 89–102 (Academic, London, 1971).
9. Barghusen, H. R. *Postilla* **116**, 1–49 (1968).
10. Hopson, J. A. & Barghusen, H. R. in *The Ecology and Biology of Mammal-like Reptiles* (eds Hotton, N., MacLean, P. D., Roth, J. J. & Roth, E. C.) 83–106 (Smithsonian Institution, Washington DC, 1986).
11. Novacek, M. J. *Nature* **358**, 192 (1992).
12. Crompton, A. W. *Proc. zool. Soc. Lond.* **140**, 697–753 (1961).

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