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# Digit reduction: via repatterning or developmental arrest?

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Hamrick (2002) contested the conclusion of our recent article on evolutionary constraints on digit numbers that in tetrapods limb reduction usually occurs via arrest of the initial development followed by degeneration (Galis et al 2001). Firstly, we agree with Hamrick that we unfortunately illustrated this phenomenon with the wrong figure: the digits in the hand of *Didelphis marsupialis* are indeed not reduced. We could have chosen many good examples in mammals (e.g., Fig. 1), and we apologize for not having done so. Fortunately, our other two illustrations of the phenomenon are good examples of the transient presence of reduced digits in amphibians (Fig. 2). Furthermore, Hamrick (2002 in press) contested the embryonal presence of a digit I Anlage in the pig (*Sus scrofa*), because he could not find such Anlagen in his serial sections. However, Baur (1884), Emery (1891, in Braus 1906), and Schmidt-Ehrenberg (1942) all have documented digit I Anlagen in the pig. In addition, both Schmidt-Ehrenberg (1942) and Holmgren (1952) confirm the presence of digit I in another artiodactyl with even more reduced digits, the cow (*Bos taurus*), and illustrate this with particularly clear drawings of the digit I Anlage (Fig. 1). The transient presence of these digits shows that reduction occurred via developmental arrest followed by degeneration. How general is this evolutionary mechanism of digit reduction?

Evolutionary digit reduction can occur via two processes, repatterning of the initial embryonal Anlage or developmental arrest possibly followed by degeneration. Lande (1978) in a review on limb reduction concluded that in amniotes, evolutionary limb reduction (including digit reduction) typically occurs by the slow continued evolution of earlier developmental arrest followed by degeneration. He documented how both in mammals and reptiles with reduced limbs the initial anlage is first developed and then regresses in absolute size (mammals: *Phocaena communis*, *P. dalli. Laegenorhynchus acutus*, and *Megaptera nodosa*; reptiles: *Python reticulatus*, *Anguis fragilis*, *O. apodus*, *Scelotes brevipes*). In the reptilian examples cell death was shown to cause the partial or entire degeneration of developed structures. Lande (1978) also documented developmental arrest followed by degeneration reduction of digits in perissodactyls (the horse, *Equus caballus*), artiodactyls (the cow, *B. taurus*), lizards (*Scelotes gronovii*), and in birds (the ostrich, *Struthio camelus*). Reviewing the digit embryology studies of Holmgren (1952), Schmidt-Ehrenberg (1942), Krölling (1934), and Kindahl (1944, 1949), we found that in all mammals that still have digits, the pentadactyl state can still be traced early in ontogeny, even in horses. Reduced digits are either permanently present as rudiments (e.g., digit II and V in cows and digit V in the hand of the armadillo *Dasypus* and the golden mole *Eremitalpa granti*) or only transiently (e.g., digit

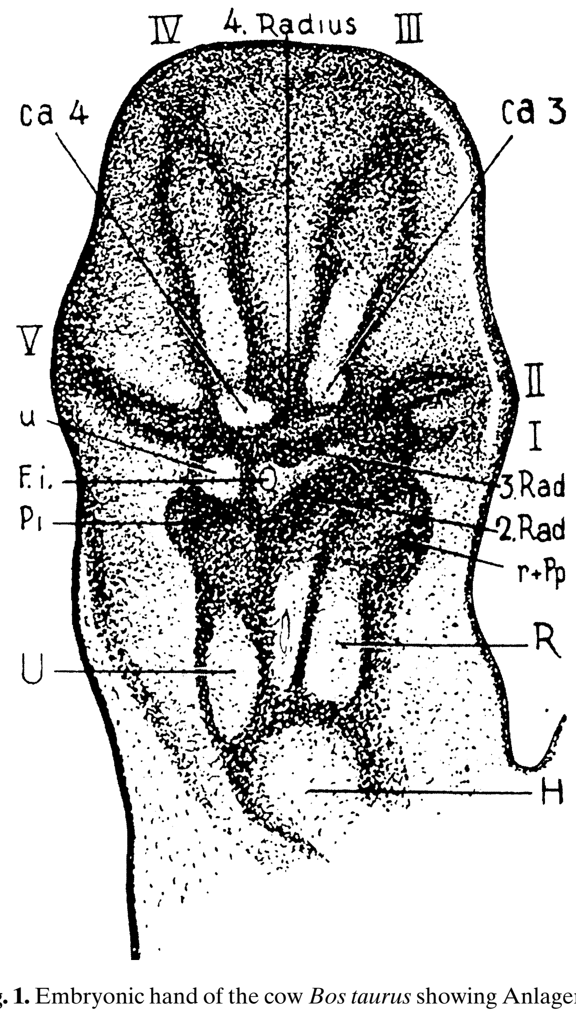


**Fig. 1.** Embryonic hand of the cow *Bos taurus* showing Anlagen of digits I to V (from Schmidt-Ehrenberg 1942).

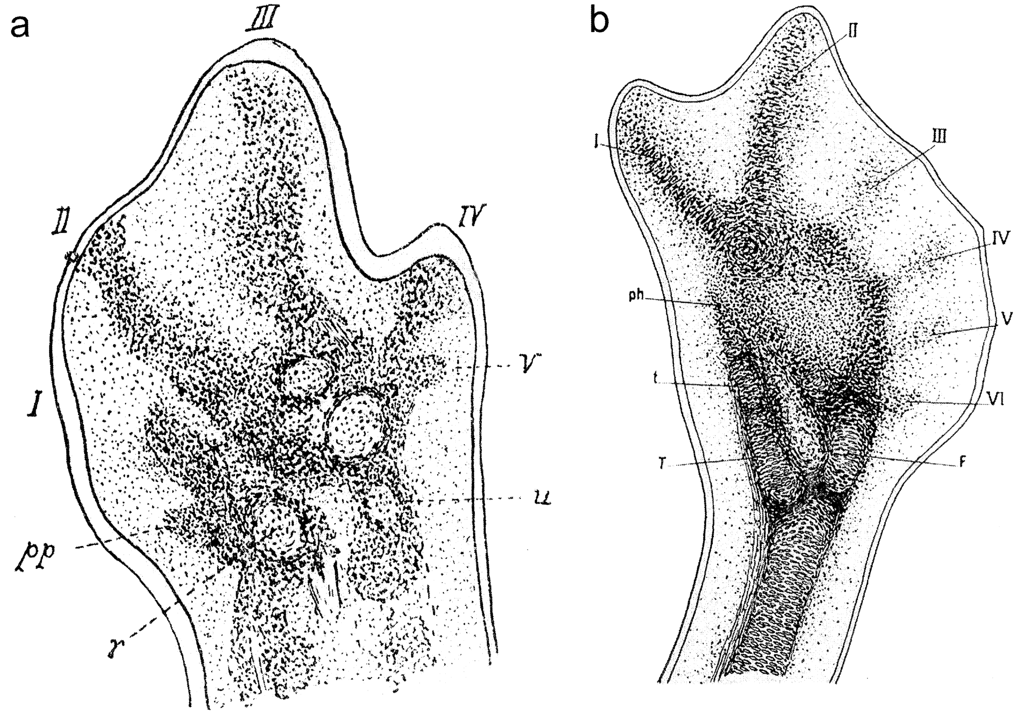


**Fig. 2.** (A) Embryonic hand of the anuran *Pelobates fuscus* showing Anlagen of digits I to V and the prepollex (sixth digit). The fifth digit is reduced in adults (from Emery 1890). (B) Embryonic foot of the urodele *Ambystoma tigrinum* showing Anlagen of six digits and a trace of the prehallux (seventh digit; from Steiner 1921).

I in the foot of *Cavia porcellus* and in the hand of *Eremitalpa granti*, *B. taurus*, *S. scrofa*, and *E. caballus*). In quite a few species a sixth digit Anlage anterior to digit I could still be demonstrated (prepollex or prehallux, Fig. 3), reflecting the more than five digits of our ancestral past. The same holds for birds. The fifth digit of avian feet is either transiently present early in development or remains as a tiny rudiment (Burke and Feduccia 1997; Holmgren 1955). In wings the fifth digit is also always present. The reduced first digit has been documented in many species (Holmgren 1955; further examples in Galis 2000). However, its presence was contested in chickens by Hinchliffe (1984), who stained for chondrification and possibly therefore missed the mesenchymal Anlage. Recent studies using new techniques now show beyond doubt the presence of the digit I Anlage in chickens and ostriches (Larsson and Wagner 2002; Kundrát et al. 2002). The authors show that the digit I Anlage passes through identical developmental events before chondrogenesis, as do other digital Anlagen of the hand. The reduction thus occurred by developmental arrest (in ostriches at a later stage than in the chicken, after some chondrification has happened). Because no traces of digit I are found later, presumably the developmental arrest was followed by degeneration.

Alberch and Gale (1985) proposed for amphibians that digit reduction is caused by repatterning of the embryonal Anlage due to a smaller size of the initial mesenchymal condensation in the limb bud. They provided developmental evidence that a smaller mesenchymal condensation indeed leads to a reduction in the number of digits. However, they did not provide evidence that the evolutionary mechanism follows the same path. In some species the transient presence of reduced digits has been documented: the fifth digit in the embryonal hand in the frogs *Pelobates fuscus* (Emery 1890) and *Bombina pachypus* (Steiner 1921), the third digit in the two-toed *Amphiuma* (Van Pée 1903; Braus 1906), and a sixth (postminimus) digit in the axolotl *Ambystoma tigrinum* (Steiner 1921). In these cases reduction has thus also occurred via developmental arrest and presumably followed by degeneration (Fig. 2).

We conclude that there is abundant evidence showing that in amniotes digit reduction occurs via developmental arrest and is usually followed by degeneration of tissues. In amphibians developmental arrest has been documented in a few species, but it is unclear whether this is a general pattern. Certainly, there no evidence yet of reduction via repatterning of the initial digit Anlage.

Lande (1978) concluded from the slowness of evolutionary limb reduction and from its pattern that the process is constrained in amniotes. Furthermore, mutations that directly cause a reduction in the number of digits in mice and humans (e.g., by reduction of the size of the initial limb bud) are associated with strong negative pleiotropic effects (Grüneberg 1963; Froster-

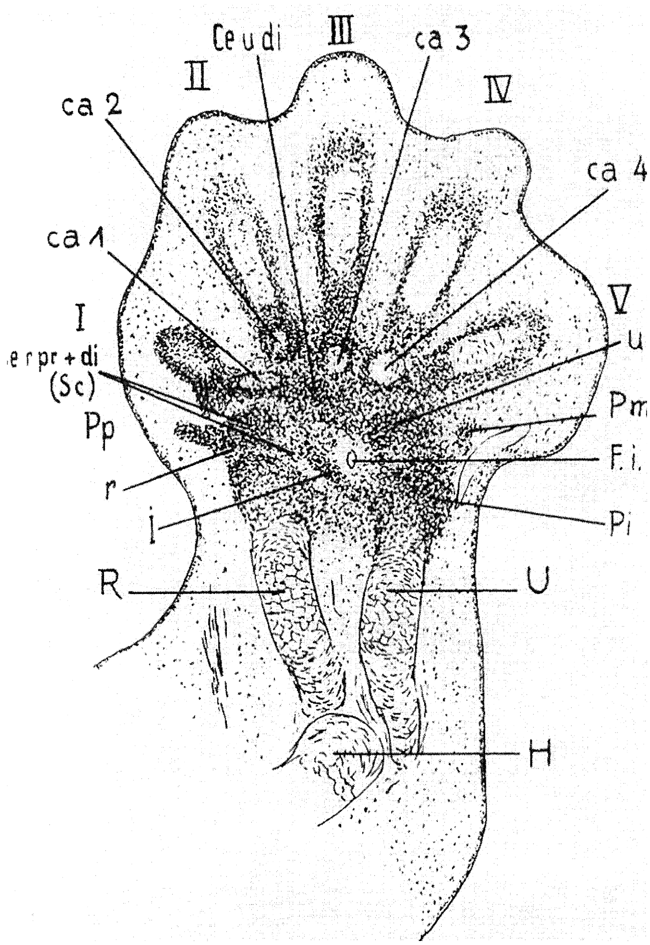


**Fig. 3.** Embryonic hand of the primate *Microcebus myoxinus* showing Anlagen of all five digits and of the prepollex (sixth digit; from Schmidt-Ehrenberg 1942).

Iskenius and Baird 1989). It thus appears that not only polydactyly is constrained due to negative pleiotropic effects (Wright 1968; Lande 1978; Galis et al. 2001) but limb reduction as well, unless it occurs via the slowly continued evolution of earlier developmental arrest (usually followed by degeneration). We hypothesized as a cause for evolutionary constraint on limb reduction that the inductive interactions of the construction phase cannot easily be missed out of the chain of inductive interactions of overall development. During the time of early digit development in amniotes (the phylotypic stage) many inductive interactions are going on in the embryo, both within the limb and between the limb and embryo (Raff 1996). The many global interactions make the stage highly vulnerable to changes because the interactiveness leads to a chain of effects in different parts of the body, pleiotropic effects in the case of mutations (Galis and Metz 2001). Limb development in amniotes forms part of the general interactiveness of the phylotypic stage. Therefore we hypothesized that the constraint on limb and digit reduction in amniotes is part of the overall constraint on changes of the phylotypic stage as a whole. (In amphibians limb development is delayed and thus more independent of the development of the remaining part of the embryo, with the expected consequences [see Galis et al. 2001].). The laborious process of limb reduction by initial development, developmental arrest, and degeneration allows limb reduction despite the constraining interactiveness of the phylotypic stage.

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