and 24 hours later in the same animals (27.5 ± 8.1 ng/ml) demonstrated a ninefold increase ($P < .02$). This effect seemed specific for naloxone. Basal prolactin levels 24 hours after implanting the cannulas in untreated control animals (7.0 ± 1.8 ng/ml; $N = 12$) were not significantly different from the values recorded prior to naloxone administration in the other groups of animals. A threefold elevation in resting growth hormone levels after naloxone administration, from 8.3 ± 3.2 ng/ml to 24.3 ± 8.5 ng/ml ($P < .05$), was also noted. These delayed effects of antagonist administration on resting hormone levels seem to have the same receptor selectivity as the morphine-induced release. Basal prolactin concentrations after naloxone injection were over threefold greater than those after naloxazone injection ($P < .05$), whereas growth hormone levels in the two groups were virtually identical.

Our results imply that the receptor mechanisms for morphine-induced prolactin and growth hormone release are different. The sensitivity of both prolactin release and analgesia to naloxazone suggests their mediation through the μ_1 sites, whereas growth hormone concentrations appear to be modulated through a lower affinity receptor. These conclusions are supported both by our data (Fig. 1) and by the data of others (*1, 2*) demonstrating a maximum elevation of prolactin at lower morphine doses than those required for growth hormone.

Naloxone's delayed action on hormone concentrations raises many questions. It may reflect a physiological rebound following the sudden suppression of hormones by naloxone (*1, 2*). However, these actions might also reflect an increased sensitivity of the system to opioids at the receptor level. Early studies of opiate receptor binding demonstrated dramatic increases in binding associated with the in vivo administration of opiates and particularly with the administration of antagonists (*13*). Perhaps this increase in binding sites is responsible for an increased sensitivity of the system to hormonal release as a result of opioid administration. It has been proposed that both prolactin and growth hormone concentrations are under tonic control by endogenous opioids (*1, 2*). Increased receptor sensitivity, therefore, would be expected to correspond with elevated basal hormone levels. This possibility also might explain why peak growth hormone concentrations after morphine administration are elevated in animals previously treated with an antagonist compared to untreated control animals. Increases in peak morphine-induced prolactin levels after naloxone treatment would not be expected in these studies since the dose of morphine used (10 mg/kg) produced a maximum response in the untreated group (Fig. 1).

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References and Notes

1. J. Meites, in *Neuroendocrinology*, L. Martini and W. F. Ganong, Eds. (Academic Press, New York, 1966), p. 669; S. M. McCann, S. R. Ojeda, C. Libertun, P. G. Horms, L. Krulich, in *Narcotics and the Hypothalamus*, E. Zimmerman and R. George, Eds. (Raven, New York, 1974), p. 121; N. Kokka, J. F. Garcia, H. W. Elliot, *Prog. Brain Res.* **39**, 347 (1973); J. A. Clemens and B. D. Sawyer, *Endocrinol. Res. Commun.* **1**, 373 (1974).
2. J. F. Bruni, D. Van Vugt, S. Marshall, J. Meites, *Life Sci.* **21**, 461 (1977).
3. C. Rivier, W. Vale, N. Ling, M. Brown, R. Guillemin, *Endocrinology* **100**, 238 (1977); L. Grandison and A. Guidotti, *Nature (London)* **270**, 357 (1977); C. J. Shaar, R. C. A. Frederickson, N. B. Dininger, L. Jackson, *Life Sci.* **21**, 853 (1977); J. B. Martin, J. Audet, A. Saunders, *Endocrinology* **96**, 839 (1975).
4. R. Simantov, M. J. Kuhar, G. W. Pasternak, S. H. Snyder, *Brain Res.* **106**, 189 (1976); S. J. Watson, J. D. Barchas, C. H. Li, *Proc. Natl. Acad. Sci. U.S.A.* **74**, 5155 (1977).
5. M. J. Kuhar, C. B. Pert, S. H. Snyder, *Nature (London)* **245**, 447 (1973); R. R. Goodman, S. H. Snyder, M. J. Kuhar, W. S. Young, *Proc. Natl. Acad. Sci. U.S.A.* **77**, 6239 (1980).
6. G. W. Pasternak and S. H. Snyder, *Nature (London)* **253**, 563 (1975); J. A. H. Lord, A. A. Waterfield, J. Hughes, H. Kosterlitz, *ibid.* **267**, 495 (1977); G. W. Pasternak, S. R. Childers, S. H. Snyder, *Science* **208**, 514 (1980); K. J. Chang, B. R. Cooper, E. Hazum, P. Cuatrecasas, *Mol. Pharmacol.* **16**, 91 (1979).
7. A-Z. Zhang and G. W. Pasternak, *Eur. J. Pharmacol.* **67**, 323 (1980); *ibid.* **73**, 29 (1981); M. C. Buatti and G. W. Pasternak, *Brain Res.* **218**, 400 (1981); S. Nishimura, B. L. Wolozin, G. W. Pasternak, in preparation.
8. Rat prolactin and growth hormone were measured by homologous double antibody radioimmunoassays with reagents provided through the Hormone Distribution Program of NIAMDD. The preparations of prolactin and growth hormone for iodination were also used as standards in these assays.
9. B. L. Wolozin and G. W. Pasternak, *Proc. Natl. Acad. Sci. U.S.A.* **78**, 6181 (1981).
10. G. W. Pasternak and E. F. Hahn, *J. Med. Chem.* **23**, 674 (1980); G. W. Pasternak, S. R. Childers, S. H. Snyder, *J. Pharmacol. Exp. Ther.* **214**, 455 (1980).
11. J. Holladay, A. Faden, G. W. Pasternak, in preparation.
12. The tail-flick assay was performed with a radiant heat source. Baseline latencies were obtained for each animal, and then these were compared to latencies for the same animal obtained 30 minutes after morphine administration. Analgesia was measured as an increase over baseline of 100 percent or greater and expressed quantally.
13. C. B. Pert, G. Pasternak, S. H. Snyder, *Science* **182**, 1359 (1973).
14. We thank J. B. Posner for assistance, A. F. Parlow and S. Raiti and the NIAMDD for their rPRL and rGH radioimmunoassay kits, and B. J. Hoffman, K. Choy, and A. Goldschmidt for technical assistance. These studies were supported in part by grants from the American Cancer Society (PDT 169) and NIDA (DA 002615) to G.W.P. and from PHS (CA 23185) to I.A.K. K.S. is a predoctoral student supported by NIGMS (P32-GM07547). G.W.P. is the recipient of an NINCDS Teacher-Investigator Award (1 K07 NS 415). I.A.K. is the recipient of a PHS Research Career Development Award (AM 00679).

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Mice Regrow the Tips of Their Foretoes

Abstract. *Mice will replace the tip of a foretoe when it is amputated distal to the last interphalangeal joint. Amputation of the digit more proximal to the joint does not result in regrowth of the foretoe. Though this growth shares certain similarities with the epimorphic regeneration of amphibian limbs, the two processes are not the same. The regrowth reported here in mice is probably similar to the scattered clinical reports of fingertip regeneration in children, and presents a model system with which to explore the controls of wound healing and tissue reconstruction in mammals.*

It is commonly believed that mammals do not regenerate their extremities in the same way that lower vertebrates or invertebrates do. Among chordates, regenerative ability has reached its zenith in the tailed amphibians. For example, most adult salamanders will regenerate a complete limb within 3 months after amputation. Initially, the limb stump is covered by an epithelium which later stratifies to a thickened apical cap as regeneration proceeds (*1*). However, if skin of full thickness is grafted over the wound this inhibits the regeneration of the limb (*2*). Accidental amputations of human fingers are often treated clinically in just this manner: the amputation surface is closed off from the environment by a sutured skin flap. The result of this surgical manipulation is a stump (*3*). Some clinicians (*3, 4*) have debrided the amputation surface, changed dressings frequently, but performed no surgical intervention. The surprising result, observed in both children and adults, has been regrowth of the fingertip.

In humans, as in metamorphosizing anuran larvae (*5*), the level of amputation

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is important. Illingworth (*3*) observed (mostly in young children) that if the finger is accidentally severed proximal to the nail, but distal to the last interphalangeal joint, the results are often cosmetically perfect within 3 to 4 months. More proximal amputations do not produce this result. However, we know nothing of the histogenesis of these tissues, nor is there any report that provides an animal model with which to explore these extraordinary observations in the laboratory. In the literature, there are very few reports over a 20-year period giving a reasonably complete description of the response to amputation in mouse or rat digits [recently cataloged by Neufeld (*6*)]. In none of the experiments were any amputations performed through the distal phalange. The amputations, therefore, were not strictly comparable to the accidental amputations reported to regrow in humans. In humans, an amputation behind the nail still leaves a substantial portion of the distal phalange and the nail bed germinal epithelium within the stump. In the mouse, the nail inserts into the digit more proximally; its posterior margin is about at the level of the joint. Therefore, the plane of amputation is critical in the mouse because an amputation behind the nail can leave little to no distal phalange, or nail bed, within the stump.

I report here that, in mice, if one is careful with the level of amputation, regrowth of the foretoe tip can be observed (comparable to that seen in children). The degree and completeness of this regrowth varies with the level of amputation with respect to the joint; distal amputations produce digits that appear more nearly complete.

Twenty B6C3H laboratory mice (4 weeks ± 2 days old) were tested for foretoe regrowth. Mice were anesthetized with an intraperitoneal injection of Nembutal, their forefeet were viewed through a stereomicroscope, and the middle digit of each forefoot was amputated with a No. 11 scalpel. The amputations were performed at two different levels on 20 left and 20 right paws. In a "level 1" amputation, the toe was severed directly behind the nail. This plane of amputation is about at the level of the joint between the distal phalange and the middle phalange. On the contralateral forepaw, a "level 2" amputation was performed; this digit was severed more proximally, through the distal one-third of the middle phalange (Fig. 1). In most instances, the tip that was removed was placed in fixative for later histological examination. In all of these animals, observation and weekly photography were concluded at 34 days after amputation and the entire digit was removed for histology. Six additional animals were subjected to the same treatment, but four of them were killed at 2 weeks and 5 days and two at 81 days.

In 16 of the 20 mice with level 1 amputations, these foretoes essentially returned to a normal external appearance (Fig. 2, A to C). The regrowth of the terminal portion of the digit (some 1.5 to 1.7 mm) was completed by about 4 weeks after amputation. These toes appeared to be complete, terminating in a fatpad. In ten of these there was no toenail. In three of six foretoes that regrew nails, the nail was abnormal in character; however, the remaining three toes that possessed nails were indistinguishable from normal. In four instances, a level 1 amputation resulted in foretoes that healed producing a stump.

In 19 of the 20 foretoes which received a level 2 amputation (Fig. 2D), the amputation surface healed over smoothly forming a blunt stump (Fig. 2E). In the remaining animal, there was a slight elongation, yet nothing comparable to the regrowth observed in level 1 amputations.

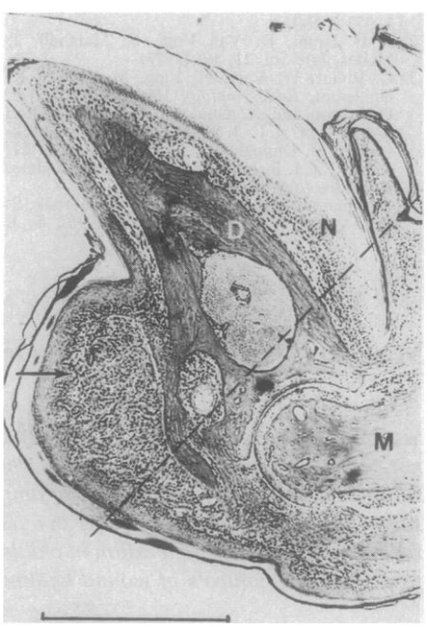

Fig. 1. A longitudinal section of an undamaged mouse foretoe. The nail and nail bed germinal epithelium (*N*) inserts at the level of the joint between the distal phalange (*D*) and the middle phalange (*M*). Note the smooth outline of the distal phalange, and the invaginations of the dermal papillae into the fatpad (arrow). The hatched line represents an approximate "level 1" amputation; a "level 2" amputation would pass through the extreme right margin of the photomicrograph. All digits were fixed in Telly's fixative, decalcified, embedded in methacrylate, sectioned at 5 μm, and stained with either hematoxylin and eosin or by the Masson's trichrome procedure. Scale bar, ~ 500 μm.

The histologic structure of all digits that did not elongate was identical to the published descriptions of other healed amputations in rodent digits (*6*, *7*). There was a proliferation of callus which capped the bone and extended down the shaft for some distance proximally. Between this callus and the covering of skin lay a connective tissue scar (Fig. 3C).

In those digits which elongated there was little evidence of a fibrocellular scar or callus formation (Fig. 3A). The remanent of the distal phalange elongated a short distance (about 1 mm) and this osseous tissue was mainly confined to the center of the digit. Subcutaneous loose connective tissue, and in a few cases, nail bed epithelium (including partial or complete nails) were observed in normal proportion past the point of amputation.

In those digits that were externally indistinguishable from normal, there was no evidence of scar tissue or callus formation, and the digits appeared complete on histological examination. There were, however, several differences between the newly reconstructed toe at 5 weeks after amputation and an undamaged foretoe. These differences, plus an examination of the foretoe tip that was originally removed, provided evidence for the plane of amputation.

The undamaged distal phalange is strongly eosinophilic and possesses a relatively smooth surface. Also, the dermal papillae of the fatpad invaginate deeply into the underlying loose connective tissue (Figs. 1 and 3B). In the reconstructed foretoe, the surface of the distal phalange is irregular (typical of new bone undergoing remodeling) and weakly eosinophilic. Moreover, no dermal papillae were observed to penetrate the fatpad. In the two animals allowed to develop for 81 days, the appearance of the distal phalange and fatpad were more similar to normal.

Histological examination of the tips that were originally amputated demonstrated that the regrowth of distal structure only occurred if a counterpart was left in the stump. In other words, complete nails did not form without a rudiment of the nail, or nail bed germinal epithelium. In toes with an apparently normal interphalangeal joint, the original plane of amputation passed through its most distal margin leaving the joint intact. Though toetips were swollen by 2½ weeks after amputation (Fig. 2B) the histologic analysis showed no evidence of a classical blastema comprised of stellate, mesenchymatous cells. Such cells

are a conspicuous feature of the formative stages of not only limb regeneration in urodeles, but in nonregenerating amphibian limbs induced to regenerate by a variety of different techniques (*8*). Within the mouse foretoe there were proliferations of spindle-shaped fibroblasts and presumptive osseous tissue arranged in whorls at the stump's end. Such a fibroblast or periosteal reaction is a common response to trauma in vertebrates (*6, 9*). However, the exact role of these cells in the regrowth of the digit awaits investigation.

Should this regrowth be referred to as regeneration? Many species of adult frogs and toads produce deficient limb structures from a more classical appearing blastema (*10*). These "regenerates" are nothing more than a spike of cartilage stemming from the severed end of the bone, surrounded by connective and vascular tissue, nerve, and skin (*11*). The regrowth of the mouse foretoe and these spikes are similar in that they both lack evidence of an epimorphic origin; however, most students of regeneration refer to the anuran limb structures as "regenerating" (*10, 11*). In some of the mice observed in this study, and in human fingers (if one judges from external morphology) a near replica, apparently functional, has replaced what was missing. Whether the regrowth of the mouse foretoe (and possibly the human fingertip) should be even loosely referred to as regeneration, I will leave to the reader; however, the regeneration of amphibian limbs and the regrowth of mammalian digits do share at least two similarities. First, in mammals and regenerating anuran larvae, the level of amputation is critical. Tadpoles, during their metamorphosis, lose the ability to regenerate their limbs. This loss occurs in a proximal-distal direction. Thus, a distal amputation will result in regeneration, whereas a more proximal amputation on the same limb will not (*5*). Can a similar gradient in regenerative ability be expressed as well in mammalian digits?

There is no simple explanation for the complete lack of regrowth above the interphalangeal joint in mice when compared to a sometimes striking and organized response to an amputation only 200 to 300 μm more distal. Moreover, in four mice discussed here, level 1 amputations did not regrow, but instead produced callus and scar. The physiological mechanisms that, on the one hand, result in callus and scar tissue formation, and on the other, allow an organized tissue response to trauma are completely unknown. Second, a skinflap inhibits the regeneration of amphibian limbs (*2*) and apparently, the regrowth of children's fingertips (*3*).

Thus, it appears that if one is careful where an amputation is performed in a mouse digit, limited regrowth will occur. These observations, together with the cyclical regeneration of deer antlers and the reports of centripetal regeneration of holes punched in the ears of rabbits (and other lagomorphs), cats, and some bats (only those that echolocate—those that fly by night vision do not regenerate ear holes) (*12*), suggest that mammalian tissue is more competent to respond to certain signals induced by injury than commonly believed (*6, 13*). Further-

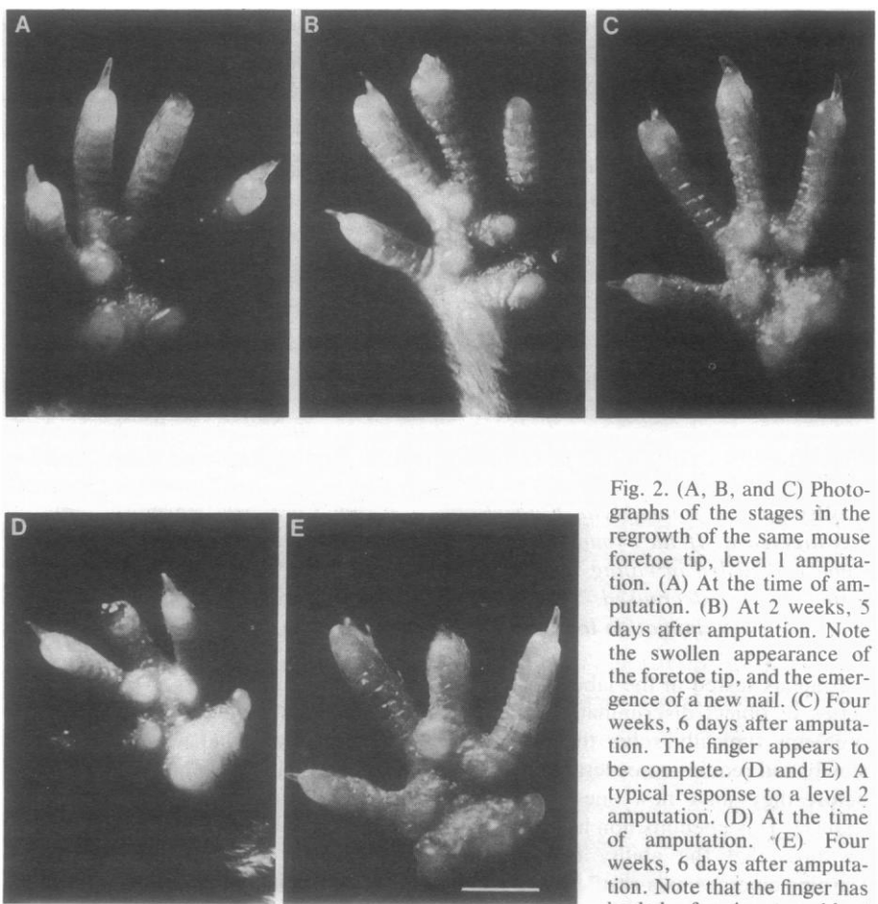

Fig. 2. (A, B, and C) Photographs of the stages in the regrowth of the same mouse foretoe tip, level 1 amputation. (A) At the time of amputation. (B) At 2 weeks, 5 days after amputation. Note the swollen appearance of the foretoe tip, and the emergence of a new nail. (C) Four weeks, 6 days after amputation. The finger appears to be complete. (D and E) A typical response to a level 2 amputation. (D) At the time of amputation. (E) Four weeks, 6 days after amputation. Note that the finger has healed forming a blunt stump. Scale bar, ~ 2 mm.

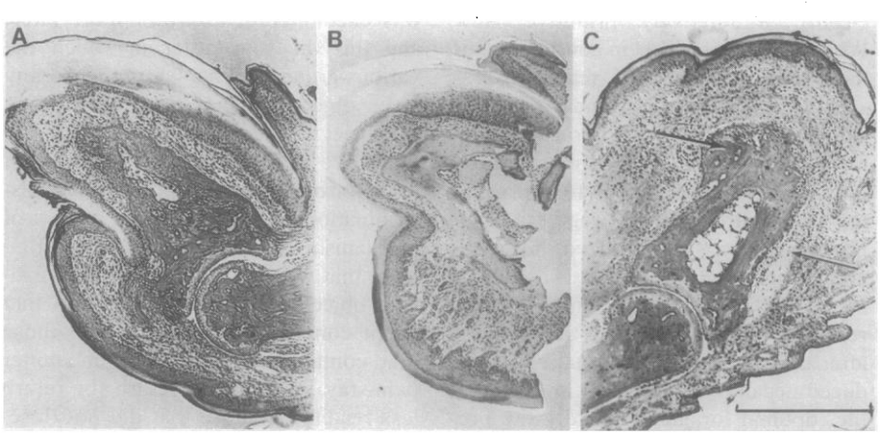

Fig. 3. Histological sections of amputated mouse foretoe tips. (A) A reconstructed tip, in response to a level 1 amputation, 4 weeks, 6 days after amputation. Note the lack of dermal papillae in the fatpad, and the irregular outline of the distal phalange. (B) A section taken from the original foretoe tip amputated from the digit portrayed in (A). Note that a rudiment of the nail bed was probably left within the stump. (C) Histological detail of a healed stump in response to a level 2 amputation. Note the callus formation (heavy arrow), the retracted severed tendon (light arrow); and the dense connective tissue between the severed end of the bone and overlying skin. Scale bar, ~ 500 μm.

more, it might eventually be possible to enhance the regrowth of less regenerative mammalian tissues once some of these signals and controls are understood.

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References and Notes

1. C. S. Thornton, *Adv. Morphog.* **7**, 205 (1968).
2. A. L. Mescher, *J. Exp. Zool.* **195**, 117 (1976). See also L. V. Polezhaev and W. N. Favorina, *Wilhelm Roux Arch. Entwicklungsmech. Org.* **133**, 701 (1935).
3. C. M. Illingworth, *J. Pediatr. Surg.* **9**, 853 (1974).
4. B. S. Douglas, *Aust. Paediatr. J.* **8**, 86 (1972); R. Farrell, W. A. Disher, R. S. Nesland, T. H. Palmatier, T. D. Truhler, *J. Am. Coll. Emerg. Phys.* **6**, 243 (1977); R. G. Farrell, *ibid.* **7**, 34 (1978); L. J. Rosenthal, M. A. Reiner, M. A. Bleicher, *Pediatrics* **64**, 1 (1979).
5. O. E. Schotté and M. Harland *J. Morphol.* **73**, 329 (1943).
6. D. A. Neufeld, *J. Exp. Zool.* **212**, 31 (1980).
7. O. E. Schotté and C. B. Smith, *Biol. Bull. (Woods Hole, Mass.)* **117**, 546 (1959). *J. Exp. Zool.* **146**, 209 (1961).
8. R. B. Borgens, J. W. Vanable, Jr., L. F. Jaffe, *J. Exp. Zool.* **200**, 403 (1977), see figure 7; O. E. Schotté and J. F. Wilber, *J. Embryol. Exp. Morphol.* **6**, 247 (1958); S. M. Rose, *J. Exp. Zool.* **95**, 149 (1944).
9. J. J. Pritchard and A. J. Ruzicka, *J. Anat.* **84**, 236 (1950).
10. R. P. Goode, *J. Embryol. Exp. Morphol.* **18**, 259 (1967). See also S. R. Scadding, *J. Exp. Zool.* **202**, 57 (1977).
11. J. N. Dent, *J. Morphol.* **110**, 61 (1962); C. M. Richards, B. M. Carlson, S. L. Rogers, *ibid.* **146**, 431 (1975). See also R. B. Borgens, J. W. Vanable, L. F. Jaffe, *J. Exp. Zool.* **207**, 217 (1979); R. G. Korneluk, M.-J. Anderson, R. A. Liversage, *J. Exp. Zool.* **220**, 331 (1982).
12. R. J. Goss, in *Mechanisms of Growth Control*, R. O. Becker, Ed. (Thomas, Springfield, Ill., 1981), p. 12.
13. R. B. Borgens, *Int. Rev. Cytol.* **76**, 245 (1982).
14. This work was performed at the Jackson Laboratory, Bar Harbor, Maine, and was supported by grant CD 32 from the American Cancer Society, Inc., NIH grant CA 20920 to R. T. Prehn; NIH grant NS 18456, and funds from the Jackson Laboratory to R.B.B. Photography assistance was provided by G. McKay and technical assistance by C. Spencer and P. Norwood.

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Marmosets (*Saguinus fuscicollis*): Are Learning Sets Learned?

Abstract. *Confronted with a novel object, a social group of marmoset monkeys investigated it. If they found food on it they returned to it readily the next day; whoever had led in eating usually did so again. If they did not find food, day 2 responsiveness decreased. These untrained performances were sufficient for one-trial visual discrimination learning.*

Animals tested in the laboratory on a series of object discrimination learning problems typically solve the first ones slowly and require considerable practice before they solve new ones in a single trial (*1*). This phenomenon has been said to show that the ability for one-trial learning emerges as a result of the training, through a special process called "learning to learn" or learning set formation (*2*). Our studies of *Saguinus fuscicollis*, a relatively primitive New World primate, suggest in contrast that if these animals have been reared in reasonably normal fashion and if the test situation is designed with consideration for their prior behavioral organization, no further practice and no formal training are required. Thus, progressive improvement in a "standardized" test situation is not necessarily the acquisition of a new ability and might simply be the regaining of previous levels of efficiency after the overcoming of situationally induced negative transfer (*3*); in everyday life, optimal foraging is hardly the prerogative of Old World primates of presumably high "general intelligence" (*4*).

Our procedure differed from those of previous investigations in that, inasmuch as most primates typically live and forage in closely knit social groups, we tested our animals in groups rather than as isolated individuals. We made only the minimum changes in their routine living conditions that were essential for assessing their differential responses to objects related and not related to food. Menzel and Menzel (*5*) found (i) that with nonfood objects family groups of *S. fuscicollis* quickly detected any novel or changed object; (ii) that they investigated only a few minutes and showed little recovery the next time the same object was encountered, a day or more later; and (iii) that the order in which the various group members approached any given object was not fixed, but varied from trial to trial according to test conditions. We hypothesized that a sufficient basis for one-trial associative object discrimination learning would be any set of mechanisms, however they might originate, that would lead animals to investigate objects or classes of objects that might contain food, to return to those that contained food on last encounter (win-stay), and to not return (or return less readily) to those that did not (lose-shift) (*6*). To demonstrate such learning without formal training we needed to incorporate into the same sort of test some objects containing food and to show that the animals immediately perform in a win-stay fashion with them while continuing to perform in a lose-shift fashion toward nonfood objects.

The social group that we tested consisted of a $9\frac{1}{2}$-year-old female, her $6\frac{1}{2}$-year-old mate, and their three sets of twins (females aged 0.60 years and males aged 1.60 and 2.35 years). All animals other than the male parent had been born and raised in captivity. None had been tested before. Preliminary training consisted of placing their customary food pan in a test apparatus rather than in its usual location and recording their behavior toward it until they seemed well habituated. The test apparatus was a 45 by 60 by 60 cm wire mesh cage with a wood floor and a 25 by 15 cm swinging door on one side. It was left in the home cage permanently and was located at a low elevation with no branches touching it. (Except at test times the animals rarely went into or onto it.) The home cage was a 3 by 4.3 by 4 m section of an indoor room, furnished with a hutch box for sleeping and a number of small trees and overhead branches. Food and water were continuously available.

The test objects were mostly household articles; they were novel to the animals and presumably easily discriminable from one another. They were randomly designated as food or nonfood objects. Jam, honey, or some other treat was smeared onto or inside of the food objects; objects had to be manipulated in different ways in order to discover what, if anything, they contained.

A successive discrimination or "go, no-go" procedure was used. First, we started a timer that produced a "beep" every 15 seconds and positioned chairs about 1 m from the home cage; one of us entered the home cage, placed a single test object on the floor of the apparatus, and closed the apparatus door. When the timer sounded again, the observer left the home cage, closed its door, and sat down. When the timer sounded again, and independently of the animals' behavior, he opened the apparatus door by means of an attached string. We recorded which individuals were on the apparatus just before the door opened (as the timer sounded), the exact order in which they entered the apparatus and took their first licks at the food, which individuals were on or in the apparatus at the moment of each timer beep, and general qualitative notes. Observation continued for $7\frac{1}{2}$ minutes; then the object was removed. A single trial was given each day and intertrial intervals were at least 22 hours.

Before putting food on any novel object we first conducted two trials with each of six nonfood objects, to assure that the animals' behavior was typical

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