The reason this mononuclear cell migration inhibition test is negative in surgically cured cancer patients is not clear. Unlike lymphocyte-mediated cytotoxicity, the lymphocyte function resulting in inhibition of migration of monocytes may require recent and vigorous in vivo lymphocyte stimulation by tumor antigen in order to maintain tumor antigen responsiveness.

The four patients with metastatic cancer undergoing chemotherapy did not show a reduction in tumor mass, and we suspect that lack of migration inhibition resulted from the effect of chemotherapy or of disseminated disease on the patients' capacity to mount a cellular immune response rather than from diminished in vivo stimulation by tumor antigen.

Removal of granulocytes, erythrocytes, and platelets from the antigen-responsive and migrating cell population used in this assay is a relatively efficient process requiring about 2 hours for cell preparation. Although its usefulness for the demonstration of cellular immunity to other solid tumors remains to be established, inhibition of mixed mononuclear cell migration correlates well with clinical status of colon adenocarcinoma and may prove to be of diagnostic and prognostic value in this condition.

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11. The authors thank Drs. C. J. DeLor, F. M. Beman, and R. M. Zollinger for providing the clinical information about their patients who were studied.
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26 February 1973; revised 7 May 1973

Behavioral Development after Forelimb Deafferentation on Day of Birth in Monkeys with and without Blinding

Abstract. *Four infant monkeys underwent somatosensory deafferentation of both forelimbs within hours after birth. Ambulation, climbing, and reaching toward objects developed spontaneously in each case. Thumb-forefinger prehension could be trained by operant shaping methods. Two infants deafferented at birth and blinded by eyelid closure were retarded in motor development by only 1 to 2 weeks. Results indicate that topographic sensory feedback and autogenetic spinal reflexes are not necessary after birth for the development of most types of movement performed by the forelimb musculature in monkeys.*

Previous research has shown that a wide range of purposive movement is possible after the elimination of spinal reflexes and somatosensory feedback accomplished by serial section of the dorsal roots of spinal nerves (*1*). Adolescent monkeys are capable of using deafferented limbs effectively for grasp, ambulation, and climbing, both while able to see and while blindfolded; they can also pick up raisins from a shallow well between thumb and forefinger. These movements are not affected by further dorsal rhizotomy; they continue to remain possible after the complete deafferentation of the spinal cord [see (*2*)].

These results indicate that the primate central nervous system is capable of generating movements of almost all types autonomously in the absence of guidance from sensory cues from the organism's own body. However, the subjects in all of these studies were adolescents with considerable motor experience prior to deafferentation. The question remained, therefore, as to whether somatic sensation is necessary in ontogeny for the development of normal patterns of coordination. The present report describes the effects of deafferentation of both forelimbs on the first day of life with and without the occlusion of vision by sewing the eyelids closed.

Four neonates (one baboon and three rhesus monkeys) were separated from their mothers within hours of birth and anesthetized. Bilateral dorsal rhizotomy (C_2 or C_3 to T_4) was then carried out intradurally under magnification (× 16; checking of the root section was at × 25 to × 40 by two observers). Intensive supportive therapy and nursing care were provided in the early postoperative period in order to

Table 1. Age (in weeks) of appearance and comparative retardation of different types of motor activity. The values are the mean ages of the first definite appearance of the behaviors.

Type of motor activity	(1) Deafferented only*	(2) Normal†	(3) Blinded deafferented	(4) Blinded only	Retardation (1) vs. (3)
Visually guided reaching	1.1	0.4			
Crouching, arms crossed	1.5	‡	2.5	‡	1.0
Sitting-crouching, arms uncrossed	1.8	0.6	4.0	0.4	2.2
Standing on all fours	2.4	.6	3.5	.7	1.1
First step	3.1	.3	4.5	.6	1.4
Sequential steps	3.3	.7	4.5	.7	1.2
Crude ambulation	3.6	2.0	5.5	2.0	1.9
Mean retardation	(1) vs. (2) = 1.8		(3) vs. (4) = 3.5		1.5

* Time of emergence of each of the behaviors was very consistent across animals in the group. † Normal data derived from Hines (*8*). ‡ This stage is exhibited only in deafferented animals.

maintain life after this long, shock-producing procedure. The completeness of the deafferentation was verified by attempting to detect summated cortical evoked responses following peripheral nerve stimulation in three animals (*3*) and by pinprick examination in all four animals (*4*). Television tape recordings were made of each animal's behavior, weekly at first and then biweekly until the age of 6 months, and at intervals thereafter.

Ambulation, climbing, and reaching toward objects developed spontaneously in all four infants. Their behavior in this regard was almost as good 3 months after birth as that of monkeys deafferented after adult movement patterns had been achieved. Grasp of small objects between thumb and forefinger did not develop spontaneously. However, the infants could be trained to perform this type of movement by means of gradual "shaping" procedures involving a series of steps of progressively increasing difficulty of performance.

During the first week of life, the infants made virtually no use of the forelimbs. A gradual improvement in motor ability then took place, reaching a peak at 3 months of age. Subsequently, the capacity to use the forelimbs regressed somewhat. For example, at 3 months of age, two infants were able to climb up a thin wire mesh (although grasp did not involve the thumb). By 4 months, grasp of the mesh was no longer observed. Similarly, a predominance of palmar placement of the hands during ambulation at 3 months (78 percent) in the baboon gave way to almost exclusive placement on dorsal surfaces of hand and wrist at 4 months (92 percent).

Some features of the data (*5*) suggest that the regression in motor ability was due primarily to the prolonged wearing of arm bandages which was necessitated by the tendency to self-inflict serious damage on the deafferented limbs by biting and sucking. The bandages prevented practice in using the digits and may have interfered with palmar placement during ambulation. With different treatment (*5*), the regression might not have taken place, and motor development might conceivably have progressed even further than the remarkable level of coordination observed.

These results indicate that in the monkey most behavior can develop after birth without any educative contribution from local somatosensory feedback. However, it remained possible that vision had substituted for the absent somatic sensation in enabling the elaboration of the observed motor development. In order to test this possibility, two further rhesus infants were given bilateral forelimb deafferentation on the day of birth combined with occlusion of vision by sewing the eyelids closed. Thus, both major sources of topographic sensory feedback (*6*) were eliminated. For the purposes of control comparison, the eyelids were sewn closed in one infant but somatosensory deafferentation was not carried out.

The results are summarized in Table 1. As can be seen, the blinded, deafferented infants developed the ability to use their forelimbs effectively for a wide variety of purposes, including supporting their body weight, walking, and clasping objects and other infant monkeys with the forearms (*7*). The emergence of these behaviors was retarded by approximately 1 to 2 weeks as compared with the infants deafferented only. However, the delay can be considered relatively slight in view of the elimination, effected by blinding, of the remaining major source of topographic feedback.

The inability to see precluded the spontaneous development of accurate reaching toward objects in the environment. However, through the use of operant shaping procedures, it was possible to train (i) precise hand-to-mouth coordination by baiting the hand with pieces of food, and (ii) discrete extension of the arm toward the front, with a tap on the upper lip as the conditioned stimulus.

These findings demonstrate that topographic sensory feedback and autogenetic spinal reflexes are not necessary after birth for the development of most types of movement performed by the forelimb musculature in monkeys. During infancy, a great deal of motor learning takes place, but the basic programs for many patterns of movement do seem to be present in the primate central nervous system at birth.

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4. The infants were uniformly very responsive to pinprick on intact portions of the body, thus rendering this test an effective method by detecting remaining sensibility.
5. When the infants were 6 to 7 months old, they were fitted with a protective suit resembling fire-fighting garb. The arms were left free, while a wire-mesh visor permitted vision but prevented the introduction of the hands into the mouth. The infants lived in these suits much of the time and were only bandaged overnight. For several hours each day, they were permitted to exercise in groups in a gymnasium that contained swings, ladders, and overhead bars, and that was designed to promote maximum motor activity. Within 1 month of the introduction of these devices, there was a marked improvement in motor coordination. Both of the animals that had not been given special training in prehension eventually exhibited grasp which, although loose and inaccurate, had previously been entirely absent. Additional results implicating the bandages in the regression of motor ability were obtained from a blind control infant in the second part of the experiment who did not undergo dorsal rhizotomy. After its hands were bandaged for several days, this infant shifted from exclusive palmar to predominant dorsal placement of the hands during ambulation. This degraded motor pattern persisted for some time after the bandages were removed, even though somatic sensation was intact.
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7. In the immediate postoperative period, one of the blinded, deafferented infants continuously maintained its phalanges in maximum flexion, exhibiting extreme resistance to extension. In order to counter this condition, the digits were passively exercised at frequent intervals throughout the day for 1 to 2 weeks, by which time the hypertonic posture of the fingers had greatly diminished. It is our impression that without this treatment flexion contracture would have developed, preventing the emergence of use of the hands. The other blinded, deafferented infant and all the deafferented-only infants also kept their fists clenched for 1 to 2 weeks after birth, but the condition was not severe enough to require passive manipulation.
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9. Supported by NIH grants MH 16954 and FR 5501RR05636. We thank Dr. David M. Rioch for many helpful comments, and Lorraine Biros for technical assistance. A portion of the data was described at the American Neurological Association meeting, Chicago, June 1972.

22 February 1973