is supported by the observation that as the animal is progressively depressed with thiopental the respiratory pattern changes from normal, frequently through a stage of couplet breathing, to respiratory arrest. Cheyne-Stokes breathing was not seen during this transition.

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Impairment of Muscle Stretch Reflexes in Tick Paralysis

Abstract. Experiments with tick-paralyzed dogs and woodchucks have shown impairment of stretch reflexes in addition to partial paralysis at the neuromuscular junction. Stretch reflexes disappear very early during paralysis, whereas nociceptive reflexes do not appear to be directly affected. The early incoordination and the ascending nature of the paralysis may be related to impairment of stretch reflex pathways.

Paralysis caused by ticks, commonly *Dermacentor andersoni* in the western United States and Canada (*1*) and *D. variabilis* in the eastern United States (*2*), is of considerable medical and veterinary importance. Paralysis is apparently caused by a toxin secreted by engorging female ticks. The progression of symptoms (see *3*) includes incoordination, muscular weakness, and flaccid paralysis. The paralysis is ascending (Landry's type); the lower limbs, the forelimbs, the cranial motor nerve functions, and the respiratory apparatus are affected sequentially. Complete recovery is rapid if the ticks are removed prior to respiratory paralysis of the victim.

Previous workers have shown failure of neuromuscular transmission during severe paralysis (*4*), and this failure has been shown to be due to a deficiency in the release of transmitter substance (*5–7*). Emmons and McLennan (*8*) have presented preliminary data which indicate that there is a central action of the toxin in addition to the peripheral action.

In the experiments herein reported (*9*), stretch reflexes were studied in three dogs and nine woodchucks (*Marmota flaviventris*) (*10, 11*) paralyzed with *D. andersoni.* Metal shields containing the ticks were taped over a shaved area of the animals' bodies (*11*). Animals were studied either at the stage of partial paralysis (incoordination of hindlimbs, little involvement of forelimbs) or of full paralysis (flaccid paralysis; slow, gasping respiration). In all cases records obtained during paralysis were compared with those obtained under identical conditions when the animal had recovered, subsequent to removal of the ticks. In some experiments pentobarbital anesthesia was used for tests during paralysis and after recovery. In two woodchucks, to avoid use of the anesthetic, the spinal cord was sectioned at the atlanto-occipital junction while the animal was under ether anesthesia. Tests were made on the paralyzed animals after elimination of the ether and were continued over an 18-hour period after removal of the ticks. Respiration and body temperature of these animals were maintained artificially.

Gastrocnemius muscle was activated by maximal electrical stimulation of the sciatic nerve. Stretch reflexes were elicited by tap of the patellar tendon or by pull of the severed Achilles tendon; controlled mechanical stimuli were delivered by appropriate solenoid devices. In some cases muscle tension was recorded on a Grass polygraph by means of a strain gauge attached to the Achilles tendon. In other experiments gross electromyograms were obtained from the muscle by means of two recording electrodes spaced 2 cm apart in the belly of the muscle (*12*).

Table 1 gives the experimental conditions and the degree of neuromuscular impairment in seven paralysis-recovery experiments. In addition, stretch reflexes alone were studied in one partially paralyzed dog and one fully paralyzed woodchuck. Muscle stretch reflexes could not be elicited in any of the paralyzed animals. Figure 1 gives representative mechanical records obtained from a fully paralyzed woodchuck and typical electromyograms from a partially paralyzed dog. It is significant that stretch reflexes were invariably absent even though neuromuscular transmission in partially paralyzed animals was only slightly reduced. Partially paralyzed animals, examined grossly, exhibited considerable muscular power. They were able to stand briefly but lacked sufficient hindlimb coordination to walk.

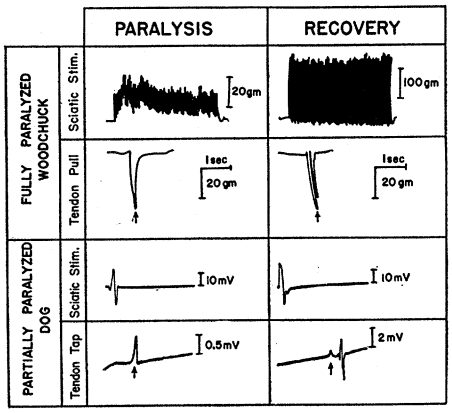

Fig. 1. Impairment of neuromuscular transmission and muscle stretch reflexes in paralysis-recovery experiments. The animals were anesthetized with pentobarbital. Arrows identify stimulus (mechanical) artifacts in records. Woodchuck: mechanical recording of muscle tension from Achilles tendon; frequency of sciatic stimulation was five pulses per second. Dog: Electromyogram recording from gastrocnemius muscle; oscilloscope traces are 50 msec in the upper row and 100 msec in the lower row.

Transmission from dorsal root to ventral root was studied in three fully paralyzed woodchucks by electrical recording techniques described previously (*13*). Two normal woodchucks were studied for comparison. The reflex discharge in normal animals consisted of a short-latency spike followed by a prolonged irregular discharge, tentatively identified as monosynaptic (2*N*) and polysynaptic responses, respectively. In one of the paralyzed animals bleeding was excessive and no transmission was observed. The ventral root discharges from the other two paralyzed animals differed from those of normal woodchucks in that the 2*N* spike was not elicited by isolated dorsal root stimuli but did appear during and following tetanic stimulation. While close comparison of such responses in normal and paralyzed animals is difficult, the results are consistent with the other evidence for impairment of stretch reflexes. In addition, since mus-

Table 1. Degree of neuromuscular impairment in paralysis-recovery experiments. EMG, electromyogram.

Animal and experimental procedure	Degree of paralysis*	Neuromuscular impairment† (%)
Dog, pentobarbital, EMG	Partial	14
Woodchuck, pentobarbital, EMG	Partial	10
Woodchuck, spinal, tension	Partial	30
Dog, pentobarbital, EMG	Full	88
Woodchuck, pentobarbital, tension	Full	92
Woodchuck, spinal, EMG	Full	77
Woodchuck, pentobarbital, EMG	Full‡	40

* Assessed from symptoms of the animal before anesthetization or section of the spinal cord. See text for criteria. † Estimated from measurements made during paralysis and again in the same animal after recovery. ‡ A 4-hour delay between the removal of ticks and the recording of the EMG allowed some recovery to occur.

cle stretch reflexes are presumably mediated by the 2*N* pathway in the woodchuck, they indicate the prominence of a central locus of action of the toxin.

Nociceptive reflexes were not quantitatively studied. Such reflexes could, however, be elicited at all degrees of paralysis. Furthermore, no evidence of impairment of polysynaptic reflex pathways was obtained from the dorsal root–ventral root experiments.

Murnaghan (*14*) and Emmons and McLennan (*8*) have recently presented data indicating that the toxin decreases conduction in peripheral nerves in addition to block of terminal branches of motor fibers (*7*). If impairment of reflexes were due only to the failure of neuromuscular transmission and to nerve block, reflex activity should be present in proportion to the degree of neuromuscular transmission. Stretch reflexes were, however, absent for all degrees of paralysis studied (see Table 1).

The present experiments do not indicate a mechanism by which such a selective block may occur. However, it is well known that the afferent fibers in the monosynaptic pathway branch extensively into fine terminals, as do the motor fibers at the neuromuscular junction. It may be conjectured that the toxin blocks fine terminal fibers at various sites in the central and peripheral nervous systems. If such is the case, its action may depend only upon the organization of the nervous pathway and not upon the type of chemical mediator released or the functions subserved.

Impairment of stretch reflexes is compatible with the symptoms of early paralysis (see *3*) and with the ascending nature of the paralysis; indeed, such symptoms can hardly be explained solely on the basis of peripheral motor block (see *6*). Incoordination, the earliest sign of impending paralysis, is not seen with curariform drugs but is observed with drugs and with surgical procedures which impair spinal reflex function. For example, interruption of afferent pathways from the hindlimbs by dorsal root section produces complete incoordination and full functional paralysis, although neuromuscular transmission is unchanged (see, for example, *12*). Thus the signs of early tick paralysis may be attributable almost entirely to the loss of stretch reflexes rather than to the slight degree of neuromuscular paralysis at this time.

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Reduction of Radiation Sensitivity of Dry Bacterial Spores with Hydrogen Sulfide

Abstract. Hydrogen sulfide reduces the lethal effect of x-rays in dry spores by about 50 percent when given after irradiation, and by approximately 75 percent when present during irradiation. The first effect is the result of removal of radicals that are toxic when combined with oxygen; the second, the removal of radicals that become toxic in the absence of oxygen. With these results we construct an explanation of the action of sulfhydryl compounds in protection against radiation damage.

With the use of dry spores of *Bacillus megaterium*, we have demonstrated the participation of free radicals and other chemical species in the lethal effect of x-rays, and the relationship of oxygen to this participation (*1–4*). Free radicals and oxygen have been discussed at length [see (*5*) for recent review] in connection with the mechanism of action of chemical compounds that protect biological organisms from the deleterious effects of high energy radiation. In this study we have tested a number of compounds related to those that are efficacious in higher organisms, and the results enable us to present a theory of the mode of action of certain protective chemicals.

It is well known that the most effective protective compounds are those containing -SH and $-NH_2$ groups. Those tested here are gases at ordinary temperatures since our system gives accurate results most conveniently with gases. In this communication we report results obtained with the simplest sulfhydryl compound, hydrogen sulfide (*6*).

The spores, mounted on Millipore filters, were exposed to 50-kv (peak) x-rays in containers that allowed control of temperature and gaseous environment as previously described (*7, 8*). Colony formation was the index of survival, with the slope of the survival line being the measure of sensitivity to radiation. Methods are described fully in other papers (*1, 2, 4, 7, 8*). In this system reproducibility from experiment to experiment is good and variances are low (*4*). The differences reported in this paper are highly significant. H_2S is not toxic to the dry spore.

In Fig. 1 the data are presented. H_2S, given to the spores after irradiation in N_2 but before exposure of the irradiated spores to O_2 (curve 3), results in protection to the same extent as that brought about by the radical scavenger nitric oxide (*3, 4*). The slope is 0.0141 kr^{-1} compared to 0.0380 kr^{-1} observed when the spores are irradiated in O_2 (*8*). When O_2 is introduced to the spores irradiated in N_2 before H_2S exposure (curve 1) this reversal is not observed, the slope being 0.0270 kr^{-1}. The interpretation is the same as for the NO results: radicals are formed that are long-lived and that can be scavenged by H_2S. These radicals become irreversibly toxic to the cell if they react with O_2.

In mixtures of H_2S and O_2, sensitivities intermediate between those observed in each alone are observed (curve 2). This preliminary result is interpreted as evidence for competition between these two molecules for the radicals in question. Detailed studies of

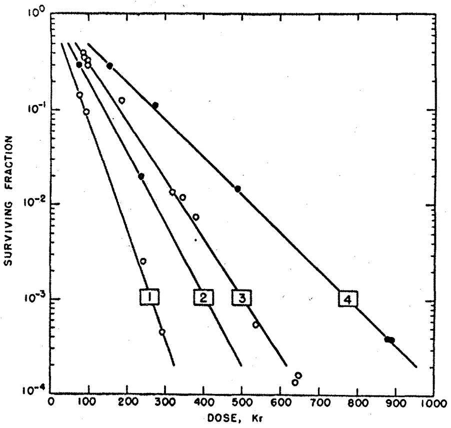

Fig. 1. Survival of dry spores of *Bacillus megaterium* when irradiated and treated as follows. Curve 1, spores irradiated in N_2, then exposed to 20 percent O_2 for 10 minutes, and then exposed to 20 percent H_2S for 15 minutes. The slope is 0.0270 kr^{-1}. Curve 2, spores irradiated in 20 percent H_2S and 80 percent air. The slope is 0.0173 kr^{-1}. Curve 3, spores irradiated in N_2, then exposed to 20 percent H_2S for 15 minutes. The slope is 0.0141 kr^{-1}. Curve 4, spores irradiated in 20 percent H_2S and 80 percent He. The slope is 0.0090 kr^{-1}.