THE CROSSED RESPIRATORY IMPULSES TO THE PHRENIC

A. ROSENBLUETH AND T. ORTIZ

From the Department of Physiology in the Harvard Medical School

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Langendorff (1887) and Girard (1890) observed contractions of one half of the diaphragm in rabbits and dogs after an ipsilateral semisection of the spinal cord above C3 and severance of the contralateral phrenic nerve. Schiff (1894) and Porter (1895) showed that the crossing of the respiratory impulses did not occur until the phrenic was cut on the opposite side. Porter further demonstrated that this crossing occurred at the level of the phrenic nuclei, not above or below.

We have failed to find any reports of further work on this phenomenon since Porter's observations. All the explanations which have been offered to account for it seem to contradict some known properties of nerve impulses or to postulate new, unparalleled properties of the nerve cells. Thus, Schiff (1894) spoke of the section of a phrenic acting as a "specific enhancing agent" of the activity of the opposite phrenic. He laid great stress on asphyxia, but did not mention the possible blocking of afferent impulses by the section. Porter (1895) suggested that some dendrites of the phrenic motoneurones cross over; the impulses they carry are not usually sufficient to cause a contraction of the opposite side of the diaphragm; but, after section of the phrenic nerve a greater portion, perhaps the whole of the "descending impulse" of that side, passes through the crossed dendrites into the phrenic cells of the opposite side. Similarly, Barcroft (1934) speaks of the impulse coming down the side where the phrenic is cut being "thwarted" along its usual path, therefore "pushing" across to the opposite phrenic along which it discharges.

The present study was undertaken with the purpose of obtaining, if possible, a satisfactory explanation of the "crossed phrenic phenomenon." We felt that before new properties are postulated for nerve cells or synapses all the possibilities of explaining the data in terms of the known properties should be exhausted. The experiments quoted did not control for the possible rôle of afferent nerve impulses and asphyxia.

METHOD. With dial (Ciba) anesthesia at the doses (per kgm.) bracketed, the following animals were used: monkeys (0.5 cc.), dogs (0.7 cc.),

1 Mexican Fellow of the Guggenheim Foundation.
cats (0.75 cc.), guinea pigs (0.5 cc.), rabbits (0.55 cc.) and woodchucks (0.6 cc.). The dial was injected intraperitoneally and supplemented with ether or urethane whenever necessary.

The vagi and phrenics were approached in the neck. For stimulation of the cut nerves, buried shielded electrodes were employed, delivering shocks from a Harvard induction coil with 5 volts in the primary circuit. Reversible blocks of the phrenics were obtained by applying pledgets of cotton soaked with ether to the dissected nerves at the base of the neck until paralysis of the corresponding hemidiaphragm was complete. The sections of the spinal cord and dorsal roots were all performed acutely. These sections were verified macroscopically at autopsy.

A tracheal cannula was inserted for artificial respiration, whenever necessary, and to produce asphyxia, either by closing the cannula or by connecting it to a rubber balloon containing nitrogen or expired air.

The movements of both halves of the diaphragm were recorded as follows. A midline abdominal incision was made from the umbilicus to the base of the xiphoid cartilage. Two long clamps were placed on the abdominal walls, immediately below the ribs. Sometimes a third clamp was fixed to the xiphoid cartilage. The clamps were lifted by a horizontal rod so that the diaphragmatic region of the animals was slightly raised from the animal board. This procedure was found not to interfere with respiration. After the abdominal viscera were pressed caudad with cotton, which also served to protect them from unnecessary exposure, the anterior half or more of the diaphragm was accessible and visible. Serrefines were then placed symmetrically toward the center of each dome

<table>
<thead>
<tr>
<th>Condition</th>
<th>MONKEYS</th>
<th>DOGS</th>
<th>CATS</th>
<th>GUINEA PIGS</th>
<th>RABBITS</th>
<th>WOODCHUCKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory hemiplegia on spinal semi-section</td>
<td>Yes</td>
<td>Yes</td>
<td>Some- times</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Crossed diaphragmatic contractions on cutting the vagi, cervical sympathetics and depressors</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Crossed diaphragmatic contractions with asphyxia (see text for exceptions)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Crossed phrenic contractions on cutting the active phrenic</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Crossed costal movements</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Unilateral costal respiration adequate</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>?</td>
</tr>
<tr>
<td>Unilateral diaphragmatic respiration adequate</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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and connected, via pulleys, to the recording levers. Downward excursions of these denote, therefore, inspiration.

This procedure was adopted for recording because it was deemed of importance to be able to observe the diaphragm directly, in order to distinguish clearly active from passive movements. Other respiratory movements such as the costal, abdominal, laryngeal and nasal, were also observed directly.

RESULTS. A. Monkeys. A spider monkey and three macaques were studied. In three of them a semisection of the spinal cord at C₇ totally paralyzed all the thoracic respiratory movements on the same side; the

![Fig. 1](http://ajplegacy.physiology.org/)

![Fig. 2](http://ajplegacy.physiology.org/)

**Fig. 1**  Macaque monkey. Left spinal semisection at C₃; complete transection at C₇. Vago-sympathetics cut. Upper record: right, and lower record: left half of the diaphragm. At lower signal, section of the right phrenic. The movements occurring after this section were transmitted from the neck and head muscles. In this and the succeeding figures the upper signal records 5 second intervals.

**Fig. 2**  Dog. Left spinal semisection at C₃; complete transection at C₇. Upper record: left, and lower record: right half of the diaphragm. Between the lower signals, section of the right phrenic.

fourth monkey will be described separately. In one of the macaques a complete transection of the cord was also made at C₇, eliminating all costal respiration. Cutting the vago-sympathetic trunks (two animals) induced only slight typical effects on the active, but no change on the paralyzed side. Section of the discharging phrenic failed in the three animals to elicit respiratory movements of the semisected side. The animal which had had the complete transection at C₇ died of asphyxia, after the larynx and nose had shown the movements which correspond to labored breathing and to gasps (fig. 1). The other two monkeys survived the section of the phrenic, the costal breathing of the active side sufficing
to maintain an adequate ventilation; they were sacrificed 40 and 60 minutes later, respectively, without having shown any further diaphragmatic contraction.

In the fourth monkey, a macaque, a left spinal semisection at C₉ failed to paralyze the ipsilateral diaphragmatic contractions, although they were smaller than those of the other hemidiaphragm. An ether block (see p. 502) was applied to the right phrenic, whereupon the entire diaphragm was paralyzed. On recovery from this block the left phrenic was cut, but the contractions of the left hemidiaphragm, which had now reappeared, were not abolished by this section. Cutting the right phrenic permanently paralyzed all the diaphragm. Obviously the contractions of the left hemidiaphragm occurred in response to nerve impulses delivered by the right phrenic, a case of peripheral crossing. With the possible exception of some cats (see section C), this was the only unquestionable instance of a peripheral crossing of the phrenic nerve supply encountered in all the animals studied. Since the ether block resulted in total paralysis of the diaphragm we may conclude that in this monkey, as in the other three, the crossed phrenic phenomenon did not occur.

B. Dogs. A spinal semisection at C₉ and a complete transection at C₇ were performed on 6 dogs; in 5 others only the semisection at C₉ was made. In all cases the diaphragm and the costal muscles were paralyzed on the side of the semisection. Cutting the phrenic on the opposite side, with the vagi intact, promptly resulted in respiratory movements of the previously paralyzed half of the diaphragm in one animal out of 3 (fig. 2). The two other dogs also belonged to the group which had a spinal transection at C₇. Cutting the active phrenic in these two animals led to immediate asphyxia; artificial respiration and severance of the vagi suc-
ceeded in bringing about adequate diaphragmatic contractions in the opposite half of the diaphragm in only one of them.

In the remaining 8 dogs the vago-sympathetic nerves were cut before section of the phrenic. With one exception, these cuts immediately led to the sharing of the previously paralyzed hemidiaphragm in the respiratory movements (fig. 3A). Subsequent section of the originally active phrenic increased only slightly the contractions of the opposite side (fig. 3B). The exception mentioned was a dog with only a spinal semisection at C₂ in which cutting the vagi did not lead to respiration of the paralyzed hemidiaphragm; subsequent section of the active phrenic resulted in slight diaphragmatic contractions on the opposite side.

In general, diaphragmatic respiration without costal participation—i.e., in the dogs with complete spinal transection at C₇—was not sufficient for adequate ventilation of the animals. Especially deficient were the dogs in which only the hemidiaphragm on the side of the spinal semisection contracted after severance of the other phrenic; they only survived for short periods.

Afferent stimulation of the cut phrenic resulted in increased and more frequent respirations in 4 out of the 5 animals in which it was tested; in the other dog slight inhibitions were observed. Strong stimuli (coil distance 7 cm. or less) were necessary to elicit these effects.
Asphyxia was produced in 4 animals by occluding the tracheal cannula during 15 to 30 seconds before severing the vagi and the phrenic. It did not result in contractions of the paralyzed hemidiaphragm.

C. Cats. Eight animals were studied. In all of them a spinal semisection was performed at C2 or C3. This semisection resulted in clear ipsilateral diaphragmatic paralysis in 3 cats only; in the other 5, movements of both hemidiaphragms were recorded, although the autopsy showed a complete semisection in at least 2 of them. The passive movements of a paralyzed hemidiaphragm (e.g., after section of a phrenic) are, however, as a rule very marked in cats. No thorough controls were made to rule out entirely such passive movements or the possibility of a peripheral phrenic crossing (see section A) in these 5 cats. We shall therefore report in detail only the other 3, in which the respiratory hemiplegia was clear.

Section of the vagi and cervical sympathetics did not produce any crossed phrenic effects. Asphyxia was likewise inefficient in this respect. Section of the active phrenic, on the other hand, resulted in crossed diaphragmatic contractions (fig. 4A). The crossing, however, did not occur promptly (cf. section E), but only appeared after a delay of from 10 to 60 seconds. The contractions of the crossed side were quite small, as compared with those of the other side before the section of the phrenic.

The detailed protocol of one of the 3 cats which showed a respiratory hemiplegia is the following. The spinal cord was semisected on the left side between Cz and Cx, and completely transected between Cs and Cx. The dorsal roots Ca, Cd and Cs were cut on both sides. The cranial nerves IX, X, XI and XII were cut on both sides. The cervical sympathetics were also cut. The right hemidiaphragm was breathing. The right phrenic was then severed, whereupon, after a delay of about 10 seconds the left hemidiaphragm started contracting. The ventilation was not sufficient, however, for the needs of the animal; artificial respiration was given; when after 10 minutes this was stopped the left hemidiaphragm again showed respiratory movements, then gasps, and the cat died.

Afferent stimulation of the cut phrenic nerves (4 animals) inhibited the respiratory excursions of the other side (fig. 4B). This inhibition was only obtained, however, with relatively strong stimuli (coil distance 6 cm. or less), weaker shocks producing no effects.

D. Guinea pigs. Three animals were tested. In two of them a right spinal semisection was made at C2. A typical respiratory hemiplegia ensued. The left phrenic was then cut; no crossed effect was obtained and the diaphragm was fully paralyzed. The left costal respiration persisted but was incapable of maintaining life; the animals died in a few minutes.

In the third guinea pig, besides the right spinal semisection at C2, a
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Complete transection at C7 was made, the dorsal roots C3, C4, C5 and C6 were cut on both sides and the vagi were severed. The left hemidiaphragm was contracting. Section of the left phrenic resulted in quick death. No contractions of the right hemidiaphragm were observed, although nasal and laryngeal respiratory movements were apparent until the end.

E. Rabbits. Observations were made on 25 animals. In all of them, the spinal cord was semisected at C2, producing a respiratory hemiplegia. In 4 a complete transection was also made at C6 or C7, paralyzing all costal respiration; the breathing movements of one hemidiaphragm sufficed to keep the animals alive.

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Fig. 5
Fig. 6

Fig. 5. Rabbit. Left spinal semisection at C2. Upper record: right, and lower record: left half of the diaphragm. Vagi cut. At signals, right phrenic cut, first below Cd, then below Cs.

Fig. 6. Rabbit. Left spinal semisection at C2. Upper record: right, and lower record: left half of the diaphragm.

A. Section of the right 6th cervical nerve.
B. Section of the right 5th cervical nerve.
C. Section of the right 3rd, then 4th cervical nerves.

Section of the vagi (13 animals), cervical sympathetics and depressors (8 animals) and carotid-sinus nerves (4 animals) failed to produce a crossed diaphragmatic activity.

Section of the active phrenic, whether the vagi were intact (6 animals) or severed (9 animals), but with uncut cervical sympathetics, depressors and carotid-sinus nerves, almost immediately resulted in respiration of the opposite, previously paralyzed hemidiaphragm (figs. 5 and 6). When the entire phrenic was not cut at one stroke, but its several roots were severed successively, the crossing over only occurred when the last root was cut, although paralysis of a considerable portion of the diaphragm resulted from the first sections (cf. fig. 2). Schiff (1894) reported that the
crossing only occurred when the component of the phrenic contributed by C₆ was cut. We failed to confirm this statement, for if the cervical nerves C₇, C₈, C₉, and C₁₀ were cut successively at their emergence from the spinal column, the crossing occurred when C₇ or C₈ was cut if the sections were made in the order stated, but the crossing only occurred on cutting C₄ if the sections were made in the reverse order (fig. 6).

When the whole phrenic nerve was cut at one stroke the crossing appeared immediately. Indeed, the first crossed contraction, though small, occurred usually at the precise time at which the other side would have contracted, had its nerve been intact (fig. 5). A gradual increase of the crossed responses appeared thereafter and in 10 to 20 seconds a steady state was attained.

The method adopted for recording is mainly qualitative. No quanti-
animal by this procedure. The results differed from those elicited by the section of the phrenic as follows. Whether the paralysis of the active hemidiaphragm occurred rapidly (5 to 10 seconds) or very gradually (several minutes), by applying various amounts of ether, the crossed contractions did not appear until practically complete cessation of respiratory activity in the blocked side. Indeed, it was possible by removing the ether opportunely to paralyze almost entirely the diaphragm without the appearance of any crossed contractions.

In contrast with the practical lack of simultaneous contractions of the two sides at the onset of the ether block, during the recovery the direct side usually started contracting before the crossed activity had subsided,
In no instance, whether after section of the phrenic or during the ether or direct current blocks, was crossed costal respiration observed. In 4 rabbits, in which both vagi, cervical sympathetics and depressors were cut before severing the active phrenic or blocking it by ether, the latter procedures did not result in crossed diaphragmatic contractions (fig. 9). In 4 other rabbits, on the other hand, an ether block was applied after severance of the vagi only, with the typical crossed effects; when the cervical sympathetics, depressors and carotid-sinus nerves were subsequently cut, the ether block now was effective in eliciting crossed contractions. These contractions, however, were delayed and smaller after than before severance of the circulatory proprioceptors. An explanation for these apparently inconsistent results will be suggested in the discussion.

Asphyxia was produced by either occlusion of the tracheal cannula or connection of it with a rubber balloon containing expired air or nitrogen. Neither procedure elicited crossed diaphragmatic contractions when performed before cutting the active phrenic or blocking it with ether (fig. 10), even if the asphyxia was carried till failure of the respiration. On the contrary, asphyxia did sometimes lead to crossed contractions when applied after an ether block had already elicited responses from the crossed side; these positive results were only obtained when the depressors or carotid-sinus nerves were intact (fig. 11).

Further tests for the rôle of asphyxia in the production of the crossed phenomenon were the following. In 3 rabbits artificial respiration was administered and the thorax was widely opened before section or block of the active phrenic. The ventilation was adjusted to very slightly less than that which would cause apnea, and was kept constant thereafter.
Section of the phrenic again evoked crossed diaphragmatic activity. In 3 other rabbits the phrenic nerves were dissected on both sides between C3 and C6 after the spinal semisection at C2. The action potentials on the active side were amplified and led to a loud speaker and a cathode-ray oscillograph, so that they could be heard and photographed. Curare was then injected in a dose sufficient to paralyze all respiratory movements. Artificial respiration was administered, and adjusted as before so that nerve impulses were rhythmically discharged through the phrenic on the direct side. The crossed phrenic was still totally inactive in these conditions. Turning off the artificial respiration for 20 to 30 seconds merely intensified the discharges in the direct side, but did not produce any crossed activity. Severance of the active phrenic below the electrodes, with constant artificial respiration, led to bilateral simultaneous discharges—i.e., the crossing occurred and the nerve impulses on the side originally active were not apparently modified. The discharges on the crossed side were not as intense as on the phrenic directly connected to the medulla.

Intermittent peripheral stimulation of the cut phrenic did not inhibit the crossed respiratory impulses (fig. 12C) unless marked hyperventilation

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Fig. 10

Fig. 10. Rabbit. Left spinal semisection at C2. Upper record: right, and lower record: left half of the diaphragm. Between signals, rubber balloon containing expired air connected to the tracheal cannula. The movements of the left hemidiaphragm were all unquestionably passive.

Fig. 11

Fig. 11. Rabbit. Left spinal semisection at C2. Upper record: right, and lower record: left half of the diaphragm. Six reversible crossings were obtained by means of ether blocks in the course of the experiment before these records were made. Vagi, cervical sympathetics and depressors cut.

A. Between signals, rubber balloon with nitrogen connected to the tracheal cannula.

B. Three minutes after A. Carotid-sinus nerves cut in the interval. Between signals, same as A.
was produced, and consequent apnea. When this hyperventilation was prevented by letting the animal breathe into a rubber balloon with expired air, no inhibition could be elicited.

Strong afferent stimulation of the cut phrenic between C₅ and C₆ was usually without influence on the respiratory activity of the opposite hemidiaphragm; in only two instances out of seven did a questionable inhibition appear. The possibility of afferent fibers in the phrenic playing a rôle in the appearance of the crossed phrenic phenomenon was further tested by severance of the dorsal roots as follows. In one rabbit a left spinal semisection was made between C₂ and C₃ and the right dorsal roots C₂, C₄, C₅ and C₆ were cut. A complete spinal transection between C₅ and C₇ was also performed. Only the right hemidiaphragm was contracting. Section of the right phrenic immediately resulted in paralysis of the right and respiration of the left hemidiaphragm. In another rabbit a similar preparation was made, but in addition the vagi were cut before severing the phrenic. Asphyxia was tested, and failed to produce contractions of the paralyzed hemidiaphragm, while section of the phrenic elicited typical results.

Other tests for afferents in the phrenic nerves were made by stimulating intermittently the paralyzed hemidiaphragms while the other side was

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**Fig. 12. Rabbit. Left spinal semisection at C₂. Vagi cut. Upper record: right, and lower record: left half of the diaphragm.**

A. At signals short tetani applied directly to the left hemidiaphragm.
B. After cutting the right phrenic. At signals short tetani applied directly to the right hemidiaphragm. The movements of this hemidiaphragm not produced by the stimuli are passive upward excursions produced by the activity of the ipsilateral costal respiration.
C. Short tetani applied to the peripheral end of the cut right phrenic.
breathing. Such a stimulation did not inhibit either the half opposite the spinal semisection, when the phrenics were intact, or the crossed activity on the side of the semisection after the opposite phrenic had been cut (fig. 12A and B).

**F. Woodchucks.** Although only two woodchucks (*marmota monax*) were successfully studied, the results are reported because they were quite clear and because of their interest in comparing them with the other species.

In one of the animals a spinal semisection was made at C2, which resulted in an ipsilateral respiratory hemiplegia. Section of the vagi elicited only slight typical effects. Section of the active phrenic was promptly followed by crossed diaphragmatic respiration. Neither central nor peripheral stimulation of the cut phrenic with various frequencies and intensities yielded inhibition of the crossed respiratory movements.

In the other woodchuck, in addition to a spinal semisection between C2 and C5, a complete transection was made between C6 and C7 and the dorsal roots C3, C4, C5 and C6 were cut on both sides. Only the hemidiaphragm on the side opposite the spinal semisection was contracting. An ether block was applied to the active phrenic, which resulted in a reversible crossing in all points similar to those obtained in the rabbits. Subsequent section of the phrenic after recovery from the ether block led to a permanent crossing of the impulses to the diaphragm. In this woodchuck also neither peripheral nor central stimulation of the cut phrenic inhibited the crossed diaphragmatic activity.

**Discussion.** The differences between the several species studied are summarized in table 1. The monkeys and guinea pigs on the one hand, and the cats, rabbits and woodchucks on the other, behaved similarly. The dogs differed from all the other species. Obviously, with such heterogeneous results a phylogenetic analysis would not be fruitful. The attempt to systematize these species differences in terms of the relative importance of diaphragmatic and costal respiration, as judged from the present data, leads likewise to inconsistent conclusions (table 1). Thus the dogs and rabbits, in which crossed phrenic effects are present, have apparently opposite relative importance of the costal and diaphragmatic respirations.

The dogs stand out as the unique species in this series, in which severance of the vago-sympathetic-depressor nerves led to crossed respiratory discharges. Quantitatively the slowing and deepening of respiration consequent upon double vagotomy was also greater in the dogs than in the other species. The larger vagal regulation of the respiratory activity of dogs may perhaps be correlated with other biological features of this animal, such as its special adaptation for running. We must, however, leave the phylogenetic aspect of the problem for further investigation.
Contradictory reports have appeared in the literature concerning the question of the effects of a spinal semisection above C₃ on diaphragmatic respiration. While some observers affirm that such a semisection leads to hemiparesis, others state that both halves of the diaphragm may continue breathing (see Cordier and Heymans, 1935, for references). Indeed, this persistence of contractions on the semisected side was once looked upon as a strong argument in favor of the existence of spinal respiratory centers.

In some species, e.g., the dogs and cats, the passive movements of a paralyzed hemidiaphragm, produced by the activity of the other hemidiaphragm and of costal respiration, are so marked that it is quite difficult, even by careful direct observation, to distinguish passive from active changes (cf. Schiff, 1894). One of the controls which Langendorff (1887) used to establish this distinction was to cut the phrenic on the side opposite the semisection, obviously a poor control in view of the knowledge acquired since. A sure method, which has not been used, however, would be to record the muscle action-potentials.

Another source of error which has usually not been duly controlled is the possibility of a peripheral crossing, such as that encountered in one monkey in the present observations (p. 498). With the exception of some of the cats (section C), on which the controls were not made to decide whether a peripheral crossing occurs or not, all the other observations made agree in showing that spinal semisection results in respiratory hemiparesis, and that in the monkeys and guinea pigs there probably is no crossed phrenic spinal path. As regards the cats, Henderson and Craigie (1936) have also recently reported respiratory hemiplegias on spinal semisections.

Crossed phrenic activity appeared in the dogs (figs. 2 and 3), the cats (fig. 4), the rabbits (figs. 5, 6, 7 and 8) and the woodchucks (section F). In the dogs, although severance of the vagi usually produced contractions of the paralyzed hemidiaphragm (fig. 3A), the fact that cutting the phrenic increased this activity (fig. 3B), and the instance in which cutting the vagi did not elicit a crossing, while section of the phrenic did (section B), indicate that there probably exist in this species phrenic spinal arrangements similar to those of the cats and rabbits. The masking vagal effects and the irregularity of the results obtained, however, make this animal unsuitable for the analysis of the phenomenon. In the cats, likewise, the results were not consistent (section C) and the effects, when present, were not very striking. For these reasons the majority of the controls were carried out in rabbits, and we shall now concern this discussion mainly with them.

When the active phrenic is cut after the spinal semisection at C₃ several effects ensue. First, there may appear a certain degree of asphyxia, particularly when the costal respiration has been eliminated by the spinal
transection at C7. Secondly, afferent impulses in the phrenic, arising at the active hemidiaphragm, might be interrupted by the section. Finally, since the paralysis of the corresponding hemidiaphragm entails changes in the expansion of the ipsilateral lung, or a cessation of this expansion when the costal respiration was eliminated, afferent impulses arising in the lung might also be interrupted by the section. These afferent impulses would travel in the nerves distributed to the lungs—the vagus and the sympathetic.

Undoubtedly relative asphyxia after section of the phrenic must have increased the number of discharges from the respiratory center in the medulla, particularly when the depressors and carotid-sinus nerves were intact. But that these increased discharges were not sufficient to elicit the crossed phrenic discharges was shown by the following controls. Asphyxia produced before severing the phrenic failed to evoke contractions of the paralyzed hemidiaphragm (fig. 10). And when the phrenic was cut while constant artificial respiration was applied after opening the thorax or under curare (p. 505), the crossing over occurred, although the discharges of the respiratory center were not modified by the section. We should therefore consider asphyxia as a probable adjuvant factor in the production of the crossed phenomenon, but not as a sufficient cause of it. The cases in which asphyxia did result in crossed contractions, when applied after previous blocks of the phrenic by ether (fig. 11), will be discussed below.

That the crossed effects are not due to the interruption by the section of a stream of inhibitory afferent impulses in the phrenic nerve is shown as follows. The phenomenon was not elicited by section of the corresponding dorsal roots (sections C, E and F), but readily occurred thereafter on cutting the remaining ventral root fibers. The possibility might still remain that these ventral root fibers include afferents, but central stimulation of the cut phrenic failed to stop the respiration of the opposite side (sections B, C, E and F). Similarly, direct stimulation of the paralyzed hemidiaphragm homonymous to the spinal semisection before cutting the phrenic, which should activate the corresponding afferents, failed to inhibit the respiration of the active side (fig. 12B).

Afferent phrenic impulses elicited by passive movements from the paralyzed hemidiaphragm before section of the active phrenie were eliminated as a source of inhibition in the woodchuck in which the corresponding dorsal roots were cut (section F), and by the controls in which the peripheral end of the cut phrenic was stimulated (fig. 12C). Such stimulation did not inhibit the crossed respiration.

Inhibitory afferent impulses in the vagi, arising at the lungs, were eliminated by section of these nerves (sections C and E). Inhibitory impulses reaching the centers by afferents in the sympathetic nerves could not have
been at play when the spinal cord was transected at C₅ or C₇ (sections B, C, E and F). Changes in such afferent impulses were further eliminated when the phenomenon appeared while constant artificial respiration was administered either with the thorax widely opened or after curare (section E; cf. Schiff, 1894; Porter, 1895).

Indeed, the time course of the crossed effects on application of the reversible ether or direct current blocks to the active phrenic (figs. 7 and 8) is such as to exclude per se both asphyxia and afferent impulses as causes of the crossing. For if either or both factors were at play the crossing should be gradual, when the paralysis is also gradual, and instead, the crossed side only enters into activity after the other side is almost completely paralyzed, regardless of the time necessary for this paralysis, and if the ether block is not complete no crossing occurs (section E).

We are led, therefore, to conclude that severance or block of the phrenic motor fibers is the necessary and sufficient cause of the crossed phrenic effects under the experimental conditions adopted. It is unlikely that a persistent antidromic bombardment of the phrenic motoneurones should be produced by the section, for the peripheral end did not discharge continuously, since the diaphragm was paralyzed on that side. The positive results of the ether and direct current blocks are further evidence against such a possibility. It appears, therefore, that the phenomenon reveals a property of neurones which differs in quality from that of conducting nerve impulses.

It was stressed in the description of the results that the events during the recovery from the ether or direct current blocks differ as a rule from those at the onset of the block (section E). While at first the crossed side does not start contracting until the originally active half is almost entirely paralyzed, during the recovery from the block the originally active side commences usually to contract long before the crossed responses have subsided. Indeed, this subsidence may take a very long time, for after an ether block had disappeared the records were never quite identical with those obtained before the application of the ether. It may be concluded that these data reveal another property of the nervous system, qualitatively different from conduction of nerve impulses. The opening of the new, hitherto unused path by the block alters the properties of the neurones or synapses involved so that they now tend to remain in use for relatively long periods of time, even though the original conditions have been practically reestablished.

This second property accounts satisfactorily for the two apparent inconsistencies observed. Asphyxia only elicited crossed contractions when a previous ether block had been applied (fig. 11)—i.e., when the crossed path had been opened at least once. Conversely, the ether block only failed to produce crossed contractions when applied for the first time after
severance of the vagi, sympathetics, depressors and (in some animals) carotid-sinus nerves (fig. 9)—i.e., when the path had not been opened before this severance—but was effective even after these nerve sections if the path had been originally opened by an early block.  

Any explanation of the crossed effects which postulates a general property of the central nervous system, without consideration of special paths, such as that of Barcroft, quoted in the introduction, should be rejected, for the phenomenon is not present in all species (table 1). Schiff's (1894) statement, that the section of one phrenic specifically enhances the activity of the opposite phrenic, is really descriptive, not explanatory. Porter's interpretation (see introduction) clearly violates the all-or-none nature of nerve impulses and is not supported by observations such as those of Gasser and Newcomer (1922), Adrian and Bronk (1928), and our own (p. 505), which demonstrate that the cut phrenic does not cease to conduct respiratory impulses.

In attempting to formulate a working hypothesis for the properties of neurone paths which the data reveal, the following considerations are pertinent. An hypothesis involving only unineuronal changes from the section or block will be preferable because simpler than one postulating influences on other neurones than those cut. It does not appear plausible, furthermore, that such changes of other neurones should occur without some causal change in the cut motoneurones. The assumption has been made (Ramón y Cajal, 1909; Eccles and Sherrington, 1931; Lorente de Nó, 1935) that neurones are not polarized as regards conduction of nerve impulses—i.e., that an impulse set up anywhere will travel throughout the cell, including the axon, perikaryon and dendrites. There is no direct evidence, however, for such an assumption. Most of the experiments which demonstrate bidirectional conduction have been made on axons; the properties of typical dendrites are very little known.

To account for the phenomena under discussion in terms of nerve impulses transmitted by the cut motoneurones we must postulate either a, that some nerve impulses, discharged continuously from the phrenic motoneurones on the intact or direct side to the crossed phrenic nuclei (e.g., by a branch of the corresponding axons) increase in magnitude after the section of the phrenic (e.g., as a consequence of electrotonus); or we may assume b, that some branches, axonic or dendritic, of the motoneurones are not accessible to cellulifugal nerve impulses until the phrenic is cut or otherwise blocked.

The suggestion a does not seem probable for the following reasons.

2 Experiments performed since this paper was sent to press demonstrate that a crossing may occur on cutting the active phrenic after severance of the vagi, sympathetics and depressors, even if no previous ether block was applied. The reason for the lack of crossing in the four rabbits reported here remains obscure.
Although a section of the motor fibers in the phrenic might change the magnitude of the nerve impulses through an electrotonic effect due to the injury potential, anesthetic blocks influence only negligibly the resting potential of nerve fibers (Bishop, 1932). Furthermore, the fact that reversing the direct current blocks (fig. 8) did not change the results argues against an explanation based on electrotonus. The direct evidence available does not support the suggestion, either, for Adrian and Bronk (1928) did not find any significant change in the action potentials recorded from the phrenic before and after peripheral section.

We might then assume, according to suggestion b, that the dendrites of the phrenic motoneurones have normally only unidirectional conduction (Gad, 1884), and that blocking the axon makes them by some unknown means capable of cellullifugal conduction, whereupon they can activate the opposite phrenic nuclei, with which they would be assumed to have synaptic connections. That dendrites may activate other neurones was a view first defended, later rejected by Ramón y Cajal (loc. cit.), but the question may still be considered open, for the evidence against such synapses is only negative.

Many other working hypotheses are possible, which would not be based on conduction of nerve impulses by the cut phrenic motoneurones. With the data on hand they would be purely speculative. The one developed is suggested only because it appears to be the simplest. On the basis of such an interpretation the data cast doubt on the assumption that nerve impulses spread normally throughout all parts of the neurones; if they did they should be active before the block or section of the phrenic; furthermore, if they did the antidromic impulses started on central stimulation of the cut nerves should activate the crossed phrenic nucleus, but they do not (sections E and F). It is of course possible, however, that this relatively simple hypothesis will prove inadequate and that changes in other neurones than those cut or blocked do occur—i.e., a change in "potential," chemical, electrical, or other, in the blocked motoneurones, might permit neighboring dendrites from the opposite side to be activated during the block.

The data obtained under curare (p. 505) lead to the conclusion that for the phenomenon to occur it is necessary to block the axons. A neuromuscular barrier such as that effected by curare is not sufficient to produce the crossing.

The two properties of the nervous system evidenced by the data—the opening of an unused path and the tendency for this path to remain open for relatively long periods—are properties which also appear in other unsolved problems of central nervous functions: the establishment of conditioned reflexes and the persistence of learned patterns. Further analysis will determine whether the similarity is meaningful.
SUMMARY

In animals of several species, under dial anesthesia, spinal semisections at Cz produced ipsilateral respiratory hemiplegias. Section of the active phrenic led to the prompt appearance of crossed diaphragmatic activity in dogs (section B), cats (section C), rabbits (section E) and woodchucks (section F). No crossed contractions occurred in monkeys (section A) and guinea pigs (section D).

Reversible blocks of the phrenic were obtained by means of ether or direct currents. These gave reversible transient crossed contractions similar to those resulting from the sections (figs. 7 and 8; section F).

The crossed effects in the rabbits, cats and woodchucks are not due to asphyxia (p. 509). They are not due to the interruption of inhibitory afferent impulses in the phrenics or vagi or sympathetics when the directly activated phrenic is cut or blocked (pp. 509, 510).

It is concluded that the crossed phenomenon reveals properties of neurone paths differing in quality from the conduction of nerve impulses: the opening of a new, hitherto unused path, and the tendency for such a path to remain open for relatively long periods of time (p. 510).

It is a pleasure to acknowledge our indebtedness to Dr. Hallowell Davis for suggesting the controls with curare and recording the action potentials of the phrenic nerves. To Dr. Henry G. Schwartz' surgical ability we owe the sections of dorsal roots in the rabbits.

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