INFLUENCE OF ASPHYXIA UPON THE RESPONSES OF SPINAL MOTONEURONS

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The information to be presented herein derives from a study of the impact of asphyxiation upon the antidromically elicited responses of spinal motoneurons in the first sacral segment. Such responses include a succession of negative deflections, m, i, b, and d, that signify impulse conduction through successive parts of the intramedullary segment of the motoneurons (the myelinated segment, the initial unmyelinated segment, cell body, and dendrites respectively) followed by certain more enduring deflections that result from the flow between parts of the motoneurons of after-currents. Details concerning these responses, their interpretation, and the means for obtaining them have been considered in two antecedent papers (12, 13) by which fact the present account is absolved from the necessity of including introductory material other than a description of method specific to the problem.

To induce asphyxiation standard procedure has been to disconnect from the decapitate, hence non-respiring, preparation the pump necessarily employed for the maintenance of ventilation. During each experiment antidromic responses were elicited and recorded at regular intervals (frequently every 2.4 seconds) throughout any period of asphyxiation, and for a variable period during recovery. The value of systematic observation and recording, a tedious procedure, cannot be overemphasized, for in casual or occasional observation during the progress of events many significant details can be overlooked. Many such details can be appreciated only after measurement of all responses in an entire series. Presentation of individual recordings for purpose of illustration necessitates the selection of but a few from the many responses elicited in any given experiment. For many purposes a graphical means of presentation suffices, it then being possible to represent, as in many of the figures that follow, all the responses of a given experimental series.

Since asphyxiation precipitates convulsions, and movement of the preparation is disastrous, curare in suitable dose has been administered. The use of barbiturates has been avoided save on those occasions that the influence of narcosis came specifically to examination.

Asphyxia and Antidromic Ventral Root Electrotonus

Description of the changes undergone by motoneurons during and following asphyxiation can begin profitably with a consideration of ventral root elec-
trotonus thereby displaying most clearly at the outset the essential mechanisms of and distinctions between asphyzial block and postasphyzial block.

Fig. 1 contains a series of records of responses to antidromic ventral root stimulation obtained by means of electrodes placed upon the stimulated ventral root, one as close to the cord junction as possible without contact, the other at a point 12 mm. from the cord junction and 34 mm. from the distal severed end of the root. With such a disposition of electrodes it has been shown (13) that normally ventral root electrotonus is recorded substantially free from distortion by ventral root fiber after-potentials. Record 1A is the normal antidromic ventral root electrotonus as described fully in an antecedent study (13). It is the resultant of intramedullary current flows due to differences in level of membrane potential in different parts of the intramedullary regions of the motoneurons. The initial negative phase relates to the metadromal current flow from axons to impulse sinks in the dendrites, the remainder relates to after-current flow initially in the direction from dendrites to axons (deflection Rp) and finally in the direction from axons to dendrites (deflection Rn). Records 1B and 1N illustrate typical changes in configuration that occur in the interval between cessation of ventilation and establishment of conduction block at the junction between myelinated and initial axon segments (cf. references 12 and 14).

Record 1B is the ventral root deflection recorded 1 minute, 10 seconds following cessation of ventilation. There has been a severe loss in amplitude of deflections Rp and Rn accompanied by some lengthening of the initial negative phase. The change that occurred between the recording of Fig. 1A and 1B usually begins about 1 minute after cessation of ventilation and is completed within some 30 seconds. Records D, E, G, and H reveal that a period of relatively little change ensues, punctuated at intervals, however, by convulsive activity easily identified by the finding, as in records C, F, and J of Fig. 1, of a blaze of asynchronous motoneuron discharge. At such times the initial negative phase and ensuing positive phase of the underlying potential change may be foreshortened only to revert in the intervals to a configuration closely akin to that seen in record 1B. As asphyxial block develops convulsive activity ceases, the initial negative phase of the sequence declines progressively, and is lost. Finally a stable positive-negative sequence is established (Fig. 1, L, M, and N).

To provide a basis for discussion of Fig. 1 it is useful to consider two facts concerning the influence of asphyxiation upon peripheral nerve: that the nerve undergoes depolarization (9, 4, 8, 15), and that the after-potentials are more sensitive than is the spike (1, 10).

Since the major electrotonic deflections (Rp and Rn) result from current flow caused by difference in after-potentials of the somata and of the axons
Fig. 1. Influence of asphyxiation upon ventral root potentials generated by antidromic volleys and recorded by electrodes placed one close to the cord junction, another 12 mm. distal but 34 mm. from distal severed end. Record A, normal antidromic ventral root electrototus. Above each subsequent recording is the time (to nearest even second) following cessation of ventilation at which it was made. Full block was established by time of record N. Time scale at bottom of Fig. 2. Negativity at proximal electrode recorded upwards.
it may be stated with confidence that the change in configuration from that of record 1A to that of record 1B is due in the main to a defect in the mechanism of after-potential production in the intramedullary parts of the motoneurons. Since, furthermore, the effect under consideration develops many times more rapidly than does the loss of after-potential by peripheral fibers (10) it is a reasonable supposition that the defect is more prominent in somata than in axons. Unfortunately a more detailed analysis of the transient change is not feasible. The electrotonus being, as stated, the resultant of different behavior on the part of somata and intramedullary axons one cannot assess the change in one part of the intramedullary motoneuron without independent knowledge of change, or absence of change, in the other. There being no doubt that the central “end” of the motoneurons undergoes significant depolarization by the time that significant change in electrotonus occurs (cf. reference 6), the intramedullary axons must be subject to a flow of demarcation current and hence changed in their properties even though the asphyxial insult itself in the direct sense may have been borne exclusively by the somata. With the introduction of the demarcation gradient in the axons themselves, the consequences of which necessarily will be recorded by the electrode pair arranged for recording of electrotonus in the normal state, the origin of whatever potential change is recorded becomes too complex for simple analysis.

Once asphyxial block is established the situation is greatly simplified and the records once more become amenable to interpretation. At the time records 1M and 1N were obtained a complete conduction block had become established at the junction between the initial unmyelinated segment and the myelinated segment of the motor axons. Accordingly, since the somata no longer are involved in true impulse conduction, it is permissible to neglect somatic contribution to recordable ventral root potential. Obviously the asphyxial block is of the depolarization or cathodal type (cf. reference 15), and the intramedullary segment of the motor axons is depolarized relative to the extramedullary stretch. With an asphyxial demarcation established at or near the cord junction the axon after-potentials at a point 12 mm. (the location of the distal lead) from the cord junction will differ from those at or near the cord junction (the location of the proximal lead), and leads so located will record the after-potential differential between the two points of contact. The potential changes illustrated in Fig. 1, M and N, are indistinguishable from ventral root after-potentials recorded in a more conventional manner (13). In the circumstance it is unnecessary to suppose that any change takes place in the after-potential of the intramedullary axon segment other than a diminution in consequence of asphyxial depolarization of that region.

Fig. 2 presents records illustrating the course of events following restoration of ventilation. It is a direct continuation from Fig. 1. Record 2A made 2
seconds after restoring ventilation is identical with record 1N. In 19 seconds
decrease in the asphyxially established root fiber after-potential proves that
repolarization of the intramedullary segment had begun. Within a few seconds
all trace of that root fiber after-potential disappeared indicating that com-
plete restoration to normal level of membrane polarization had taken place.
Record 2C was obtained just after normal membrane potential must have
been reattained. During the ensuing 12 seconds an entirely new potential
sequence was established and had reached its maximum amplitude (Fig. 2,
D and E). At such time following reventilation the recorded potential is
negative for some 60 msec., but finally reverses into a prolonged positive
phase. Further recovery appears to take place in two stages. In the first of
these, represented by records F, G, and H of Fig. 2, there occurred a progres-
sive recession of the postasphyxially established potential sequence that reached
its peak in records D and E of Fig. 2, so that at a point of time between rec-
ords H and J of Fig. 2 the configuration of recorded ventral root potential
essentially reduplicated that of record 2C. Then, some 2 minutes after com-
mencement of reventilation, begins the final stage of recovery in which (record
2J) the first unequivocal sign of the returning preasphyxial electrotonic poten-
tial can be distinguished and during which (Fig. 2J to P) the return to normal,
or preasphyxial, electrotonus was completed. Record 2P is indistinguishable
from record 1A indicating full recovery in so far as electrical response is a
criterion.

From experiments of a different sort (cf. Figs. 9 and 10) it is known that
many motoneurons, frequently 25 per cent of the total at a given instant,
are capable of conducting antidromic impulses at a critical stage during the
transition from the status obtaining at the time represented by record 2B to
that obtaining at the time represented by record 2D, and that complete block
is reestablished when the root potential has acquired the configuration seen
in record 2D. It is certain from the potential records that the intramedullary
block established within 30 seconds of reventilation must be quite different
from that prevailing at the onset of reventilation. The only available ex-
planation is that the level of membrane potential which had begun to rise
just before record 2B was made, and which had reached normal just before
record 2C was made, then continues to rise to some value which is greater
than normal before again approaching the normal level. In other words,
oxidative repolarization in the intramedullary motoneurons displays a post-
anoxic (postasphyxial) overshooting just as does peripheral nerve according
to the descriptions of Lorente de Nó (15).

Since impulses do not penetrate into the motoneuron somata by the time
the recorded ventral root potential has the form reproduced in Fig. 2D and
E it is proper to refer that potential form to action of axons. It must be sup-
posed, then, that the potential as recorded in 2D and 2E results from the
Fig. 2. Postasphyxial change in ventral root potentials. This is continuation of Fig. 1. Record A, ventral root potential 2 seconds after restoring ventilation. Subsequent recordings at the stated times (to nearest even second) following reventilation. Normal antidromic ventral root electrotonus restored in record P.

after-potential differential between the hyperpolarized intramedullary axon segments and a normal region of their extramedullary ventral root extensions. Despite this rather complex origin the resulting potential closely resembles
the type of after-potential recorded by Lehmann (10) from peripheral nerve in the postasphyxial state.

According to the evidence presented it may be concluded that asphyxial block is associated with various signs of central depolarization and may therefore be likened to a cathodal block, that on reventilation the cathodal type of block is relieved with extraordinary rapidity only to be replaced by another block which, being associated with signs of hyperpolarization, may be likened to blocks of the anodal type. Thus a distinction must be drawn between "asphyxial block" and "postasphyxial block."

To what extent the damage wrought by asphyxia is repaired by the time that membrane potential recovers is not known. If the decline of membrane potential is the sole cause of asphyxial block then it would follow that asphyxial block is relieved completely in a matter of seconds and that the postasphyxial overshooting is a sufficient explanation for the occurrence of postasphyxial block. If, on the contrary, any significant fraction of the motoneuron population suffers through agencies other than depolarization then to the extent that such other agencies might persist into the period after the motoneurons are repolarized the nature of postasphyxial block would be complex. Nevertheless, the role of membrane overshooting in postasphyxial block is emphasized at this time for it does not seem to be recognized generally that recovery from asphyxia is not simply a repair of the asphyxial defect. With suitable reservations it may be said that eventual recovery is not so much recovery from the asphyxial state as it is recovery from the postasphyxial state.

**On a Method for Locating Conduction Blocks in the Circumstance of Conduction in Volume**

Fig. 3 contains records made by means of electrodes placed, for A and C, at the ventral root entry zone to record the response of intramedullary axons (spike m) and, for B and D, at a point in midsegment just dorsal to the denticulate ligament to record the response of dendrites (deflection d). Records A and B of Fig. 3 illustrate the normal responses as earlier described (12). After obtaining those records the preparation was asphyxiated until such time as a complete conduction block had developed as indicated by the complete absence of deflection d in record 3D. At that time the response recorded from the ventral root entry zone had the configuration shown in observation 3C. It is seen that the recorded magnitude of spike m is enhanced enormously.

Enormous increase in antidromic responses of motoneurons during asphyxiation has been described (3) and attributed to relief of conduction blocks. Such an explanation, undoubtedly applicable to the experiments cited, cannot be invoked in the present instance in which the increment in recorded response amplitude pertains to the response of axons. Furthermore, it is difficult to
imagine that the records of Fig. 3 reflect at one and the same time relief of a block and imposition of a block. Since other instances are known in which increase in magnitude of a deflection recorded in volume is associated with depressed response (12) it has seemed advantageous to study the development of block in a peripheral nerve located in volume to provide a simple model upon which to base analysis of change in the more complex situation provided by spinal motoneurons.
When a nerve in volume is blocked, as by the action of cocaine, an impulse volley is recorded at the upper margin of the block as a diphasic potential change, positive-negative in sequence, indicating the approach and arrival, but non-departure of that volley. Beyond the block a positive deflection is recorded indicating a flow of current from points beyond the block to the blocked sinks. An observation of particular utility for present purpose concerns the sequence of changes in form of the response recorded at the upper margin of a developing block during the period of that development. Fig. 4 illustrates the observation. To obtain the records of Fig. 4 a peroneal nerve was so arranged that its middle stretch lay in volume. One end of the nerve, in insulating medium, rested upon electrodes fitted for stimulation. One recording lead was placed upon the nerve near the midpoint of its stretch in volume. The input circuit was completed through another lead in the volume at a distance from the nerve. A few crystals of cocaine then were placed on the nerve at a point beyond the first mentioned lead. Without further manipulation the records of Fig. 4 were obtained. A hazard of the experiment is that the action of the cocaine may spread to the locus of recording rather than remaining confined to a region below that locus, with attendant reduction of the recorded negative phase of the action. Since movement during the application of cocaine may alter slightly the conditions of recording, the initial record was made immediately after rather than before the application.

Observation 4A consists of the triphasic response to be anticipated in recordings of impulse volleys in midvolume. In the subsequent records, B to E, the metadromal phase is lost progressively as increasing numbers of fibers

![Fig. 4. Cat peroneal nerve in volume. Recordings by electrode upon nerve at midvolume pitted against distant electrode. Record A, normal. Subsequent records show changes occurring as a cocaine block develops at a point just beyond recording site. Record E, block complete.](image-url)
fail to conduct impulses through the treated region. Prodromal positivity, in accordance with expectation, is unaffected throughout. The second (negative) phase, however, is seen to increase in amplitude and duration pari passu with loss of the metadromal positive phase.

Given the fact that the negative phase in volume increases in front of a block and decreases beyond it, it is a simple matter to predict what will happen in varying circumstances. For instance, if a conduction block were to travel through a region under observation the event would find expression in an initial rise and subsequent fall in amplitude of the negative phase. Similarly the existence of a fluctuating block could be detected by the finding of reciprocally linked rises and falls in amplitude of response at two successive points that straddle the fluctuating block in a conduction pathway.

**Asphyxia and Intramedullary Anoxic Responses: the Location of Asphyxial Block**

It is apparent that the observations of Fig. 3 made at the axonal and dendritic extremities of the intramedullary parts of the motoneurons are insufficient to define the precise location of asphyxial block. To secure more critical information it is necessary to observe the responses at intermediate points along the intramedullary segment.

Contained in Fig. 5 are records made with the aid of a microelectrode inserted to a point within the spinal cord at which the conjoint \(i,b\) (cf. reference 12) deflections are recorded in consequence of ventral root stimulation. Record A was obtained at the time of cessation of ventilation and records B to M were made at the stated intervals following that time. Records N to Q were made at the stated intervals after restoration of ventilation. For a period of about 3 minutes following the cessation of ventilation (5B to 5E) little change in the \(i,b\) elevation was in evidence, although a slight increase in the succeeding \(d\) elevation can be noted. Then, in fairly rapid course (5F to 5M) the entire response decreased. Asphyxiation was not carried to the extent of producing complete block. Following restoration of ventilation the early response returned rapidly and overshot the normal amplitude (5N to 5P). During this early phase of recovery one cannot determine from the records whether deflection \(b\) as well as deflection \(i\) had recovered. Later, however, (5Q) the distinction between \(i\) and \(b\) clearly was reestablished, and the response as it appeared before asphyxiation was restored in approximation.

Following recovery from the asphyxial bout represented in Fig. 5 the microelectrode was advanced a fraction of a millimeter ventrad until spike \(m\) came into view, whereupon the preparation was reasphyxiated, and the records of Fig. 6 obtained. The observations contained therein were selected so that Fig. 6 would compare with Fig. 5. During the 1st, 2nd, and 3rd minutes following the cessation of ventilation spike \(m\) changed little (6A to 6E). Then, as asphyxia was prolonged into the 4th and 5th minutes, spike \(m\) increased
progressively in magnitude and duration (6F to 6M), but, since the asphyxiation was not prolonged unduly, spike m, as recorded in observation 6M, presumably was not at the attainable maximum. Parenthetically it might be stated that continuation of asphyxia will result eventually in the disappearance of spike m, but the augmented status of spike m is maintained for a period prior to the onset of final decrease. Upon restoring ventilation the asphyxially augmented spike m rapidly decreased in amplitude (6N to 6P), but it was only much later that control amplitude was regained (6Q).

By concentrating attention upon changes wrought by asphyxia in the amplitudes of spike m and deflection i it is possible to represent, within a reasonable space, all the recordings made during periods of asphyxia and subsequent recovery. The method is graphical, the amplitudes of successive responses, elicited each 2.4 seconds, being plotted as a function of time fol-

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**Fig. 5.** Asphyxial (records B to M) and postasphyxial (records N to Q) change in conjoint, i b deflection. Record A is the normal response to antidromic ventral root stimulation. Times (to nearest even second) from onset of asphyxiation given below each record A to M and from reventilation below each record N to Q. Time base above record L in 0.2 and 1 msec. intervals.
Following cessation of ventilation. Fig. 7, A and B, present instances in which amplitude change of spike m was observed during and following an asphyxial bout. During the first minute of asphyxiation spike m is quite stable in amplitude, but thereafter some fluctuation is evident written most frequently, as in 7B, upon a slowly progressive increment in amplitude (cf. also Fig. 11A).

The most notable feature, however, is the final rapidly progressive augmentation of spike m that, in 7A, reaches an obvious plateau. Following reestablishment of ventilation, at times indicated by arrows, spike m decreases precipitately, but incompletely, through a short lived minimum (marked ×) after which a slow phase of recovery begins. Control amplitude usually is reattained only after some 20 to 25 minutes.

To be found in Fig. 7, C, D, and E are presentations in detail of the be-
FIG. 7. Asphyxial and postasphyxial change in amplitude of spike $m$ (A and B) and of deflection $i$ (C, D, and E). In each plot zero time signifies the onset of asphyxiation whilst an arrow signifies restoration of ventilation. Records obtained each 2.4 seconds from onset of asphyxiation, recorded amplitude in each record represented by a point in curve.

Behavior of deflection $i$ during and following a period of asphyxiation. Deflection $i$ in the normal course of events appears to be less stable than is spike $m$ and, upon asphyxiation, and following a latent period, it fluctuates in magnitude more noticeably than does spike $m$. After the period of fluctuation
deflection \( i \) declines more or less rapidly to extinction. A slight preterminal rise may be seen, as in Fig. 7C, indicating that the developing block may shift in position. Reventilation following the advent of complete block brings about a sudden resurgence of deflection \( i \), frequently with a brief recession (marked \( \times \) in Fig. 7D) at about 20 seconds of recovery time. Deflection \( i \) then rapidly overshoots its resting magnitude before entering upon a final slowly progressive return to normal. The final recovery stages of spike \( m \) and deflection \( i \), in each instance from a greater than control amplitude, follow closely similar temporal courses.

**Interpretations.**—The observations of Figs. 5, 6, and 7 find their interpretation in the model experiment discussed in connection with Fig. 4. Conjoint increase in spike \( m \) and disappearance of deflection \( i \) demonstrate that asphyxial block to antidromic conduction in motoneurons is established, and remains for a time, at the junction of the \( m \) segments and \( i \) segments of the motoneurons, which is to say at the junction of the myelinated and initial segments of the intramedullary axons. The present conclusion thus recapitulates that enunciated by Lorente de Nó in his study of the hypoglossal nucleus (14). It does not accord with the assumption of Brooks and Eccles (3) that asphyxial block resides at the axon-soma junction.

If the preparation is reventilated following establishment of block between \( m \) segments and \( i \) segments, that block, following a brief latent period, is relieved promptly. Abrupt decrease in spike \( m \) and restoration of deflection \( i \) document the event. It is now apparent that the postasphyxial block not only differs in nature from the asphyxial block, but also that it is located at another and more central point in the motoneurons, which point necessarily is somewhere in the somata proper. Failure of spike \( m \) to return completely to normal and the overshooting of deflection \( i \) beyond normal amplitude are events related to the development of that somatic postasphyxial block just as the asphyxial increment in spike \( m \) alone is related to the development of intraxonc asphyxial block.

The downward discontinuities labeled \( \times \) in Fig. 7 are caused by the fact that a certain number of motoneurons are capable of conducting impulses at any given instant during a critical stage of the transition from cathodal type, intra-axonc, asphyxial block to anodal type, intrasomatic, postasphyxial block.

**Asphyxia and Somatic Responses**

**Concerning Deflection \( b \).**—Observation of asphyxial change in deflection \( b \) is made difficult, and analysis of it uncertain in meaning, by the fact that deflection \( b \) always in some degree is underlaid by deflection \( d \) whenever recorded by an electrode so placed that deflection \( b \) is the initial negative deflection following prodromal positivity (12). For the same reason it is futile to attempt graphical representation of change inflicted upon deflection \( b \). Nevertheless some
information can be gleaned from observation of deflection \( b \) during asphyxiation. Fig. 8 presents several recordings from a series obtained, by means of a penetrating (extracellular) microelectrode, from a region in which deflection

\[
\begin{align*}
&b \quad d \\
&0' \quad A \\
&1' \quad B \\
&1'50'' \quad C \\
&2'24'' \quad D \\
&3'42'' \quad E \\
&4' \quad F \\
&4'12'' \quad G \\
&40'' \quad H \\
&48'' \quad J \\
&1' \quad K \\
&1'25'' \quad L \\
&2'30'' \quad M
\end{align*}
\]

**Fig. 8.** Records to show asphyxial and postasphyxial change in deflection \( b \). Record A, normal conjoint deflection. Records B and G, changes during asphyxiation. Records H to M, changes after restoration of ventilation. Times (to nearest even second) after onset of asphyxia and after restoration of ventilation.

\( b \) stood as the initial negative deflection, during (records 8A to 8G) and following (record 8H to 8M) a period of asphyxiation. As recorded normally (record 8A) deflection \( b \) continues with little discontinuity into deflection \( d \).

To judge by the appearance, in records 8A to 8D, of the ascending limb of deflection \( b \) little change occurred during the first 2.5 minutes following cess-
tion of ventilation. In the meantime change in deflection $d$ resulted in the two deflections nearly becoming confluent. Discussion of asphyxial change in deflection $d$ except to the extent that it beclouds the present issue is deferred until consideration of Figs. 9 to 15. During the 4th minute of asphyxiation (8E and 8F) response failed progressively and by the time of record 8G was blocked. Without attempting too rigid an analysis it may be said that deflection $b$ disappears about the same time following cessation of ventilation as does deflection $i$.

Latency for beginning postasphyxial recovery of deflection $b$ (8H and 8J), when considered in conjunction with the observations, in Fig. 7, D and E, on recovery of deflection $i$, would appear to include the time required for deflection $i$ to overshoot its resting level. Thus the first locus of the postasphyxial anodal type block is presumably the axon-soma junction.

The rate at which deflection $b$ recovers following asphyxiation cannot be estimated in a satisfactory manner, nor is it possible to conclude the presence or absence of an overshooting such as that undergone by deflection $i$. A comparison of records 8A and 8M, for instance, immediately reveals that the underlay by deflection $d$ is very different in the two instances so that any consideration of amplitude at a given stage of recovery in terms of normal amplitude is meaningless. Considered by itself record 8M indicates that a fair degree of recovery of deflection $b$ had taken place during the first 2.5 minutes of reventilation. In the circumstance a case could be made for supposing that the postasphyxial block regresses spatially as well as temporally.

Concerning Deflection $d$, the Response of Dendrites.—Much of the available information concerning the behavior of deflection $d$ during and following asphyxiation can be presented in graphical form based upon measurements of amplitude. In fact for the most part that is the method of choice for the presentation of sample recordings cannot possibly convey in reasonable space an impression of the swiftly paced and fleeting changes that the relatively labile response of dendrites undergoes.

Figs. 9 and 10, in which amplitude of deflection $d$, the response of dendrites recorded at midsegment and dorsal to the denticulate ligament, is plotted as a function of time following cessation of ventilation, illustrate the course of asphyxial change and, in part, the course of postasphyxial change in the response of dendrites. Deflection $d$ is a response that exhibits considerable fluctuation in amplitude, even as do monosynaptic reflexes, when elicited by infrequent rhythmical stimulation. Exhibiting that fluctuation deflection $d$ is found not to be influenced very markedly by asphyxiation until some time during the 2nd minute following cessation of ventilation. A slight rise in amplitude may take place (Figs. 9, 11, and 14), or a slight fall (Fig. 15), or, indeed, no change may be measurable (Fig. 10). Then, and without other
Fig. 9. Plot of asphyxial and postasphyxial change in recorded amplitude of deflection d. Asphyxiation begun at zero time, reventilation at the arrow. Records each 2.4 seconds from onset of asphyxiation.

Fig. 10. Similar to Fig. 9, but from another preparation. A, block develops suddenly preventing preterminal rise which is seen in B. Plot A represents the first asphyxiation this preparation had experienced, plot B the second imposed after long recovery period.
premonitory sign, a period of more or less wild fluctuation is entered upon. Frequently these fluctuations bring response amplitude to a greater than preasphyxial level, as in Figs. 9 and 10 (also Figs. 13 to 15). On the other hand, if the response has declined the fluctuations may succeed only in restoring amplitude to the neighborhood of preasphyxial level (Fig. 11). However that may be, the short lived recurrent augmentations of deflection d are apparently the counterpart of asphyxial convulsions.

Following the period of convulsions deflection d may decline rapidly to extinction (Fig. 10A), but by far the more usual course of events is that it begins slowly and progressively to rise in amplitude to a maximum that is not maintained for more than a few seconds before the onset of final failure (Figs. 9, 10B, also 11, and 13 to 15). For ease of description the terms “convulsive increments” and “preterminal increment” of deflection d will be introduced. The events they describe are not comparable.

Following restoration of ventilation, at times indicated by arrows in Figs. 9 and 10, there occurs regularly a transient and fractional relief of block (marked x in Figs. 9 and 10, also in Figs. 14 and 15) that recedes, usually completely, before a slow, progressive, and enduring relief commences. A notable feature is that final recovery in recorded amplitude of deflection d takes place initially at a fairly rapid rate and then more slowly until after 20 or more minutes it is complete.

The simplest explanation for the observed convulsive increments of deflection d is that they compare in nature with the increase of recorded somatic response, originally described by Renshaw (16), that occurs when an antidromic response of motoneurons is caused to fall intercurrent upon reflexly aroused synaptic bombardment. In an earlier study (11) this form of increased response was shown to relate to an increase in the number of antidromic impulses that could penetrate from the region of short refractory period to the region of more prolonged refractory period. More recently (12) it has been shown that it is in penetration of the b segment of the motoneurons that antidromic impulses acquire the more prolonged refractory period, hence, increased penetration of somata is an important contribution to the increase in recorded response brought on by reflex stimulation.

Now, if the “convulsive increments” of deflection d do indeed represent increased penetration by antidromic volleys of motoneuron somata then it follows that each such increase in recorded amplitude of deflection d should necessarily take place in concert with a decrease in recorded amplitude of axonal response. The test of this proposition is simple and the result unequivocal. It has been noted in connection with Fig. 7 that certain irregularities or fluctuations in axonal response took place after the 1st minute of asphyxiation. In order to relate those with fluctuations in deflection d, if relation there be, it is necessary only to record axonal (spike m) and dendritic (deflection d)
responses simultaneously by means of the double oscillograph during a period of asphyxiation, and to plot the result in the manner of Fig. 11. It will be seen that each convulsive increment in deflection $d$ is associated with a "convulsive decrement" in spike $m$. For this reason it is concluded that the convulsive increments of deflection $d$ do in fact represent increments of somatic response. It is otherwise during the preterminal rise of deflection $d$.

If, in consideration of Fig. 11, attention is directed not to the convulsive fluctuations but rather to the underlying trend it will be noted that spike $m$ begins to increase in the 2nd minute of asphyxiation as deflection $d$ is diminishing and that the axonal spike continues to increase during the pre-

Fig. 11. Plots of simultaneous asphyxial change in spike $m$ (A) and in deflection $d$ (B). Broken lines added to emphasize the coincidence of decrements in spike $m$ and increments in deflection $d$ during convulsive period.

terminal rise in deflection $d$. About 15 seconds before the preterminal rise of deflection $d$ has reached its peak the rate of increase in spike $m$ increases sharply to become maximal at least 7 seconds before deflection $d$ is at the peak. In short the preterminal rise in deflection $d$, far from being an expression of actual increase in response, must be a sign of growing asphyxial deficit.

Another approach to the analysis of the preterminal rise in deflection $d$ can be made by comparing, in simultaneous recordings, change in deflection $d$ and in the metadromal positivity of spike $m$. It was shown earlier (12) that the metadromal positivity of spike $m$ represented axonal sources of current flow to impulse sinks in more central parts of the motoneurons, including the dendrites. Fig. 12 presents records obtained from the caudal limit of the root entry zone (left column) to display the metadromal positivity of spike $m$ and
FIG. 12. Records of left column made by means of electrode at the caudal limit of ventral root entry with amplification adjusted to display metadromal positivity of spike m. Records of right column made by means of electrode dorsal to denticulate ligament at midssegment to display deflection d. The pairs of records (A₁ and A₂ etc.) were made simultaneously by double recording. A, records, preasphyxial responses. B to F, records, selected from complete series to illustrate asphyxial change during period of preterminal increment in deflection d and subsequent decline.

from the lateral surface to display deflection d (right column). At the amplification employed spike m could not be recorded in its entirety.

Records A₁ and A₂ of Fig. 12 were obtained at the time of cessation of ventilation, records B₁ and B₂ during the preterminal rise of deflection d,
which deflection had reached its peak at the time records C₁ and C₂ were made. Three stages of the terminal decline of deflection \( d \) are depicted in the D, E and F records respectively. Despite the fact that deflection \( d \) is shown, in Fig. 12, first to rise and subsequently to fail in magnitude, in the succession of records of the left column the metadromal positivity of spike \( m \) is seen merely to decrease. If the records of the left column had been made at lesser amplification to permit full observation of spike \( m \) that spike would be found to increase progressively in the successive records A₁ to F₁ in much the same fashion as it is seen to increase in duration. Progressive increase in the pro-dromal positivity of deflection \( d \) in records A₂ to F₂ may be correlated with progressive increase in spike \( m \). The conclusion again is that the preterminal

![Graph](https://example.com/graph.png)

**Fig. 13.** Plots of asphyxial change in recorded amplitude of deflection \( d \) in response to the first of paired shocks (dots) and to the second (crosses). The ventral root stimuli were separated by an interval of 4 msec.

rise in deflection \( d \) must reflect the development of an asphyxial defect rather than an increment in response.

Yet another distinction between the nature of response in the convulsive increments and the preterminal increment can be made upon the basis of the ability of dendrites to carry two impulses in relatively rapid succession. The experimental result presented in Fig. 13 deals not only with this question, but has somewhat broader interest in the analysis of response to asphyxiation, and accordingly the discussion of it must be more general.

It is by now well known that certain parts of the motoneuron soma in the usual course of events are incapable of conducting fully the second of two volleys coupled in rapid succession (16, 11, 2, 12, 13). Evidence has been presented (12) to the effect that the dendrites rather than the cell body are the weak point in the conduction path and that hyperpolarization following
response is the mechanism by which conduction of a second volley is prej-
udiced. In the experiment illustrated by Fig. 13 the dendritic response,
deflection $d$, to the second of two volleys separated by an interval of 4 msec.
attained an amplitude approximating 25 per cent that of response to the first
volley of the pair. Dots chart the course of asphyxial change in the response
to the first volley, whereas crosses do the same with respect to the second.

During the initial minute of asphyxiation no significant alteration in re-
sponse is noted. Then, and within less than 20 seconds, deflection $d$ in re-
sponse to the second volley increases to the point that it nearly equals in
magnitude the response to the first volley of the pair. Reference to the ob-
servations discussed in connection with Fig. 1 discloses the fact that the
asphyxial increase in the second of paired dendritic responses takes place at
the time when recordings of ventral root electrotonus reveal the development
of a severe defect in the mechanism of after-potential production by the
motoneuron somata. In other words, the dendrites in suffering the loss in
their normal after-potential mechanism acquire the ability to respond more
fully to iterated excitation within a short space of time.

Then follows the period of convulsions, and it is abundantly clear that the
second of the paired responses experiences convulsive increments at the same
times as does the first response.

As asphyxiation proceeds and the first of the paired dendritic responses
enters into the preterminal rise the dendrites rapidly lose the ability to con-
tribute a second response. At the peak of preterminal rise recorded amplitude
of the second response is but 7 per cent that of the first and a few seconds
thereafter the second response is quite absent. In brief, from the very onset
of the preterminal increment in deflection $d$ the recovery process of the den-
drites is so deficient that they exhibit a Wedensky type of inhibition that is
not evident in otherwise similar circumstances up to the onset of the pre-
terminal rise in deflection $d$.

It is important to reemphasize the distinction between the normal failure
and the preterminal asphyxial failure of dendrites to carry two volleys in
succession. Normal failure is of the anodal type due to overshooting of mem-
brane potential following conduction. The asphyxial failure is of the cathodal
type due to reduction in the rate of recovery of membrane potential.

Recovery of the dendritic response following restoration of ventilation is
remarkable principally for the short lived ability of the neurons to conduct
impulses as they pass from the state of asphyxial block to that of postas-
phyxial block. Magnitude of the response that appears at the peak of transient
relief of block (marked $\times$ in Figs. 9, 10, 14C, and 15B) is variable: in one
instance a response 57 per cent of preasphyxial magnitude was recorded.
It is legitimate to presume that not all the motoneurons would perform their
repolarization and overshoot at precisely the same rate so that at any given
instant not all the motoneurons would be in precisely the same state. Accordingly it is interesting to speculate to the effect that all motoneurons at some instant in the course of repolarization are capable of conducting fully and that the actual magnitude of recorded response merely indicates the number of motoneurons that find themselves at the critical state of recovery at the instant they are called upon to conduct a test volley.

It has been noted that final recovery of dendritic response amplitude from the condition of postasphyxial block takes place initially at a rather high rate and then more slowly (Figs. 9, 10, and 14C). The initial phase of final recovery in which deflection $d$ increases relatively rapidly is usually completed well within 2 minutes of the reestablishment of ventilation. Reference to Fig. 2 indicates that this more rapid phase of increase in deflection $d$ takes place in parallel with recession of the postasphyxially established ventral root potential sequence (Fig. 2D), and that the change to a slower rate of amplitude increase in deflection $d$ coincides in time with the beginning reappearance of the normal pattern of electrotonus (Fig. 2J), which is to say with the onset of recovery of the somatic after-potential mechanism.

The foregoing correlation is of interest for it suggests that the actual course of increase in deflection $d$ during recovery from postasphyxial block may be as illusory as is the preterminal rise during the asphyxiation itself. This is not to imply that recovery is not taking place from the time that deflection $d$ begins to emerge, but rather to suggest that the increase in deflection $d$ as recorded may represent a combination of circumstances one of which is progressing relief of postasphyxial block, the other, perhaps, a fortuitous increment related to the failure of dendrites to become sources for after-current flow during the initial phase of recovery.

Asphyxia and Augmentation of Antidromic Response

With the exception of the brief fluctuating convulsive increments of dendritic response no evidence has been forthcoming to support the notion that asphyxiation leads to an augmentation of antidromic response of spinal motoneurons. Since, in a comparable study, Brooks and Eccles (3), who incidentally did not report the occurrence of convulsive increments of response, describe the antidromic soma spike as increasing enormously in size during asphyxiation to exceed in all experiments the preasphyxial response by 400 to 600 per cent, a search has been made for the conditions under which progressive augmentation of response may occur. It seemed fairly obvious a priori that forcing the dendrites by one means or another into a severely depressed state might set the scene for subsequent augmentation of response during asphyxiation.

Depression by Prior Asphyxiation.—Fig. 14 illustrates an experiment in which the preparation was subjected to repeated asphyxiations. Amplitude of
the dendritic response, deflection \( d \), has been plotted. An initial asphyxiation (14A) was carried to the stage of complete asphyxial block, after which the preparation was ventilated for 32 minutes during which time recovery progressed to apparent completion. The preparation then was reasphyxiated to the point of block (14B) with no striking difference in the course of events other than a shortening of the blocking time. From this second asphyxiation only 3.5 minutes' recovery was permitted (14C) before the preparation was reasphyxiated (at the time of the arrow in 14C). Now, deflection \( d \), in the 2nd minute of asphyxiation, is seen to increase in a progressive fashion, this in contrast to behavior in more normal circumstances. It would appear in this instance that reasphyxiation in the course of depolarizing the motoneurons acts initially by removing the postasphyxial hyperpolarization block. It is of interest to note that the motoneurons have been seen to go through the entire asphyxial cycle when reasphyxiation began only 24 seconds after prior complete asphyxial block, at which time the postasphyxial block was complete.
Depression by Narcosis.—Fig. 15 illustrates the distinction between asphyxial change in deflection \( d \) in the decapitate, but otherwise normal preparation, and in the narcotized preparation. During the experiment illustrated nembutal (ca. 20 mg. per kg.) was injected intravenously at some time between the observations on the left and those on the right. In consequence of the nembutal depression deflection \( d \) underwent a striking progressive increase in amplitude during the 2nd and 3rd minutes of asphyxiation and the convulsive increments, present prior to narcosis, failed to appear. In other words, the course of events came to resemble more closely the description as given by Brooks and Eccles (3) whose preparations likewise contained nembutal. Barbiturate depression resembles an anodal depression in the sense that it is relieved rather than reinforced by the depolarization attending asphyxiation.

On the Blocking Time of Spinal Motoneurons

With asphyxiation induced by cessation of ventilation the time required for the development of complete block has usually not been less than 3 minutes (but cf. Fig. 7E) nor more than 4.5 minutes. Repeated asphyxiation sometimes (Fig. 14A and B), but not always (Fig. 10A and B), reduces the blocking time. Blocking time in the present series of experiments thus is about equal to the survival period for reflexes according to van Harreveld (5) who employed a slightly different technique. On the other hand, Brooks and Eccles (3) report their enormous asphyxial augmentation of antidromic response as reaching its peak in 5 to 10 minutes with response disappearing only within another 1 to 4 minutes.
A number of attempts have been made during the present study to prolong the asphyxial blocking time. Several barbiturates have been employed, but in no instance did barbiturate narcosis prolong significantly the time for development of asphyxial block (cf. for instance Fig. 15). In fact the only effective means found for extending the latent period for block is lowering of body temperature. In a specific experiment at 38.5°C. latency was 4 minutes, 20 seconds. After injection of nembutal, 30 mg. per kg., and a fall of temperature to 38°C. it was 4 minutes, 33 seconds. On reducing temperature to 33°C. blocking time became 6 minutes, 20 seconds. The most prolonged blocking time encountered has been 7 minutes. Attempts at further prolongation were abandoned.

DISCUSSION

Depolarisation of the Spinal Cord in Asphyxia.—It is of interest to discuss the present experiments in relation to those of van Harreveld upon asphyxial depolarization in the spinal cord (5–7). Employing the same technique of respiratory arrest herein employed it was noted that depolarization began on the average 52 seconds after respiratory arrest, which is close to the time that obvious change begins in ventral root electrotonus, or that the second of two closely spaced dendritic responses begins to increase in magnitude. In other words, the after-potential mechanism of the motoneuron somata is severely damaged in a matter of seconds after the onset of depolarization.

On restoring ventilation van Harreveld found that the latency for beginning repolarization on the average was 20 seconds. In the present experiments latency for beginning reversal of asphyxial block is close to this figure, but if anything shorter, for the peak of the temporary relief of block occurs between 20 and 24 seconds after beginning reventilation and, in the experiment of Fig. 2A, significant change in the ventral root potential had occurred in 19 seconds. From the present evidence one would estimate that membrane potential passes through the normal after no more than approximately 24 seconds' reventilation.

The origin of the potentials described by van Harreveld must be rather more complex than supposed for only rarely was there any sign of the postanoxic overshoot that is so constant a feature in the present experiments, and of nerve tissue behavior generally. True, from the present evidence, the intramedullary stretch of the motoneurons (axon as well as soma) is more uniformly influenced during the hyperpolarization of postasphyxia than during the depolarization of asphyxia. If, as is suggested, the method of van Harreveld is peculiarly sensitive to axon-soma difference, then presumably the overshoot would be a less spectacular facet of his recordings.

On Augmentation of Response and Normal Behavior.—True augmentation of response in the central nervous system may take place at synapses through
recruitment from a subliminal fringe, or elsewhere by relief of conduction block. There is evidence to the effect that certain motoneurons may be blocked at the axon-soma junction by the time that an experimental preparation has been completed and observation begun. There is absolutely no evidence that such a block exists in the animal as distinct from the experimental preparation. A conservative view of asphyxial relief of axon-soma blocks, then, would be that they occur in degree inversely proportional to degree of excellence of the preparation.

It seems on many counts that the dendrites of motoneurons are delicately poised with respect to their capacity for impulse conduction. Indeed this feature may be of considerable importance to the manner of their functioning in the central nervous system. In the course of experimental examination one becomes impressed by the fact that their capabilities differ at different times, at different places, and for different reasons. In a crude sense one may regard dendrites as tapering structures so thick usually at their origin as to defy definition of a body-dendrite junction, but becoming eventually the finest of threads. It is legitimate, if futile at present perhaps, to argue whether or not true conduction normally continues to the very tips of such structures (cf. reference 14). Nevertheless, in the experimental preparation impressive augmentation of their response brought on by one or another means is impressive evidence of derangement. Despite the fact that normal response of dendrites has yet to be defined, one must bear in mind the possibility that even in the “best preparations” the performance one registers may fall something short of normal. And so, in consideration of asphyxiation, although one may grant that an early phase of hyperexcitability may lead to augmented reflex responses (5) through recruitment from a subliminal fringe, it is something else to infer that conduction blocks are normally of common occurrence at one or another point of intramedullary neurons waiting only to be relieved by asphyxiation, or some other intervention.

On the Location of Blocks to Antidromic Conduction.—The location in motoneurons, and in one or another circumstance, of blocks to antidromic conduction is a problem much discussed in recent years (16, 11, 14, 2, 3, 12, and many others). Present remarks will be confined to the proper theme of this investigation.

According to presently available information the primary asphyxial block is located with reasonable certainty at the region of junction between initial and myelinated segments of the motor axons. Location of the postasphyxial block cannot be so narrowly defined. At the outset it appears to involve the entire soma, which is to say that an axon-soma block develops upon reventilation as the intra-axonic block is relieved. From then on the most reasonable supposition would be that the postasphyxial block recedes progressively from the point of impulse entry into the soma towards the dendrite tips. That
supposition is not entirely fanciful. It is known that dendritic conduction is prejudiced by hyperpolarization since the hyperpolarization that follows prior response can cause a major deficit in subsequent response. Furthermore, it has been shown (reference 12, Fig. 16) that the post-response deficit involves a gradient of decrement within the dendrites such that degree of penetration varies with intensity of the post-response process. It is to be expected that postasphyxial block, also having its origin in hyperpolarization, would behave in similar fashion.

CONCLUSION AND SUMMARY

Observations have been made upon asphyxial and postasphyxial changes in the electrical responses of motoneurons to antidromic stimulation. Analysis has been aided by the use of a simple method for locating conduction blocks in the circumstances of volume conduction. Asphyxiation has been produced by suspending artificial ventilation. Regular practice has been to restore ventilation immediately after complete conduction block is established. This has permitted study of the postasphyxial state, but not of the effects of prolonged asphyxiation with the latter of which this paper is not concerned.

With asphyxiation produced in the manner outlined a latent period of approximately 1 minute precedes the onset of asphyxial change. The initial change, to judge by the work of others (6, 7), is beginning central depolarization. At the same time there is a severe loss of somatic after-potential (Fig. 1). Through this loss the dendrites acquire the ability to carry two volleys in rapid succession (Fig. 13). These changes appear to reach completion within approximately 30 seconds. There follows a period of convulsive activity during which reciprocal amplitude changes in the response of axons and dendrites prove that a fluctuation in somatic responsivity is taking place (Fig. 11). Intermittent impulse discharge in ventral roots is seen (Fig. 1). Conduction block may be developing slowly throughout the period of convulsive activity (Fig. 11). Frequently there is a rather definite instant at which convulsive activity ceases and a rapid development of block begins. Usually the recorded amplitude of the dendritic response then increases to a peak (the preterminal increment) before final disappearance (Figs. 9 to 11, 13 to 15). A variety of reasons has been advanced to show that this preterminal increment represents not increased response, but rather a developing block (Figs. 11 to 13). When fully established, asphyxial block is located at the junction of the initial and myelinated axon segments (Figs. 5 to 7). It is a depolarization or cathodal block.

On restoring ventilation a latency of less than 20 seconds antecedes the onset of postasphyxial change. Within the span of a few seconds membrane potential recovers and overshoots the normal level. At a critical stage of repolarization motoneurons are capable of conducting impulses, but again lapse into block
The newly established block is due to hyperpolarization and is anodal in type. It is a somatic rather than an axonal block. Final recovery from the postasphyxial block requires some 20 minutes. As soon as motoneurons perform the rapid transition from asphyxial block through normal to postasphyxial block they will, upon reasphyxiation, pass through a new and complete asphyxial cycle with the one difference that a marked phase of incrementing response is experienced due to asphyxial mitigation of the post-asphyxial block (Fig. 14).

Barbiturate narcosis depresses the response of dendrites in a manner that resembles anodal depression for it is relieved rather than reinforced by asphyxial depolarization (Fig. 15). Asphyxial augmentation of response may acquire spectacular dimensions when written upon a state of barbiturate depression.

Blocking time of the spinal motoneurons is on the average about 3.5 minutes. It may be shortened by prior asphyxiation (Fig. 14) and is lengthened by cooling of the preparation. Narcotization has not been observed to alter survival time significantly (Fig. 15).

BIBLIOGRAPHY


