

THE EXTINCTION OF REFLEXES IN SPINAL MICE OF
DIFFERENT AGES AS AN INDICATOR OF THE
DECLINE OF ANAEROBIOSIS

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I

The following experiments were undertaken as part of an investigation of the possibility of the occurrence of partial anaerobiosis in newborn and suckling mice. Several other methods of approach, such as asphyxiation by illuminating gas or by carbon monoxide (Enzmann and Pincus, unpublished) or by nitrogen (Kohn, unpublished data) have been studied and the results will be presented elsewhere. It has been noticed in all these experiments on asphyxiation that young mice exhibit a remarkable resistance to lack of oxygen, which is in agreement with the results of earlier experimental work on similar lines (Bert, 1874; Avery and Johlin, 1932; Irving, 1933; *et al.*). It occurred to us to initiate asphyxiation through stopping the blood supply to the spinal cord by transecting it at the mid-region of the cervical spinal column, definitely below the level of the respiratory center. A similar method has been used to produce anemia in definite regions of the central nervous system (Stenson, 1667; Pike, 1909; and other workers). The result of interrupting the blood supply to the spinal cord is a gradual disappearance of all reflexes and final paralysis.

II

The head was severed from the body by transecting the neck with a sharp pair of scissors in the region indicated. The method is not ideal as it involves a variable amount of bleeding, but is preferable to a blow on the head. Stunning and killing the animals by a sharp blow on the head usually leads to severe internal hemorrhages, which might interfere with reflex activity after the initial shock; furthermore, a blow cannot easily be delivered with equal force or always at the same point, and for some reason it leads to a more severe shock than transection of

the spinal cord. The timing was done with a stop-watch. The reflex activity was tested by means of mechanical or graded electrical stimulation.

In the description of the phenomena following the transection of the spinal cord at the mid-cervical region we shall make use of some of the terms employed by Riddoch (1917), but we shall define the term "spinal shock" as a temporary stopping of all reflex activity of the spinal cord below the level of the transection immediately after the operation.

Four sharply defined periods may be distinguished after the transection, which are characterized by the appearance of the following phenomena:

1. Immediately following the operation there is *shock* ("period of flaccidity" of Riddoch), during which the animals are perfectly quiet although various groups of muscles, notably those concerned in flexion of the spine, show strong contraction.

2. There follows a period of *hyperirritability with spontaneous mass reflexes*, chiefly vigorous kicking of the hind legs and convulsive twitching of the tail; the forelegs are not always involved.

3. The period of *mass reflexes*. The animal is perfectly quiet, all spontaneous motions having disappeared. The nervous system is still hyperirritable and each single stimulus throws the whole body into convulsive activity. This period passes gradually into a period of orderly responses resembling those obtained in the spinal frog, although the reflexes are less purposeful. As the spread of nervous impulses diminishes, the animal gradually enters the last period, that is, failure of reflexes.

4. The final period, *failure of reflexes*, is characterized by a gradual decline of the reflex activity. While during the preceding period every stimulus causes results in movements of both fore and hind legs, the spread now is much less. Gradually the area from which reflexes may be obtained diminishes, until only stimulation of the base of the tail and upper part of the hind legs leads to response. The threshold increases enormously, while the vigor of response declines till somatic death supervenes.

III

There are remarkable age differences in each of these periods, especially in the last one. The period of shock is very brief in all animals but is definitely shorter in very young mice. The recovery is quicker

in newborn than in adult and more complete, extending to the forelegs in every case. It is noted that the shock is severest in the vicinity of the lesion. The differences in duration of this period with the age have not been studied in detail because the method of timing with a stop-watch does not permit an exact definition of such small differences. The period of spontaneous mass reflexes lasts longer in young animals and is more complete. The differences in duration of this period between young and adults are also not large. The greatest differences

TABLE I

Duration in seconds of the periods during which reflexes may be obtained from spinal mice of various ages at room temperature (about 22°C.).

Age in days after birth	Mean duration of reflex periods	No. of observations
	<i>sec.</i>	
0	1270	8
1	922	11
2	731	6
3	650	7
4	610	2
5	476	4
6	408	2
7	338	6
9	207	2
12	148	22
15	68	18
18	47	9
30	39	4
40	33	3
120	34	6

are obtained during the last two periods. In newly born mice reflexes may be obtained by stimulation of the skin for about 1,300 seconds following transection of the cord, while in adult animals all reflexes die out in 20 to 40 seconds. The duration of the periods during which responses may be obtained from spinal animals at room temperature is shown in Table I and in Fig. 1. The duration of the periods during which reflexes are obtainable from spinal animals declines sharply during the 1st week of life and more slowly during the 2nd week. The adult level is reached at or before the 3rd week after birth.

The curve representing the experimental results closely resembles that obtained by Kohn (unpublished data) for asphyxiation of young mice with nitrogen, and by Enzmann and Pincus for asphyxiation with illuminating gas, which supports the view that in the extinction of reflexes in spinal mice we are dealing essentially with the same problem as in asphyxia.

In the first series of experiments the temperature of the young animals was not measured. It is known that the onset of paralysis in cold blooded animals after clamping the abdominal aorta and depriving the lower spinal cord of oxygen, appears much slower than in

TABLE II

Duration in seconds of the periods during which reflexes may be obtained from spinal mice of various ages at a controlled temperature ($37.5^{\circ}\text{C.} \pm 0.5^{\circ}\text{C.}$).

Age in days after birth	Mean duration of reflex periods	No. of observations
	<i>sec.</i>	
0	1040	22
1	880	16
2	679	13
3	596	7
4	585	21
6	473	5
7	322	11
10	176	6
12	145	4
14	78	6
40	42	8

warm blooded animals subjected to the same treatment. It is also well known (*cf.* Pincus, Sterne, and Enzmann, 1933) that newly born mice are practically poikilothermic and that the apparatus for the regulation of the body temperature develops only gradually.

In order to take these facts into account a second set of experiments was arranged. Young mice of various ages from birth to 40 days of age were kept in an incubator at $37.5^{\circ}\text{C.} \pm 0.5^{\circ}\text{C.}$ until their body temperature, judged by applying a thermometer to the skin, approximated that of adult mice kept under the same conditions. The results are shown in Table II and Fig. 1. It appears that the deficiency of the

temperature-regulating mechanism in young mice is indeed a factor of importance. The curve obtained by strict control of the temperature is during the 1st week of life in every instance below that obtained at room temperature. The curve is less steep; the differences in the duration of the reflex periods between newly born and adult mice, however, are significant, and disprove the hypothesis of Barrows (1933) that the difference between newly born and adult mice is due to a difference in body temperature.

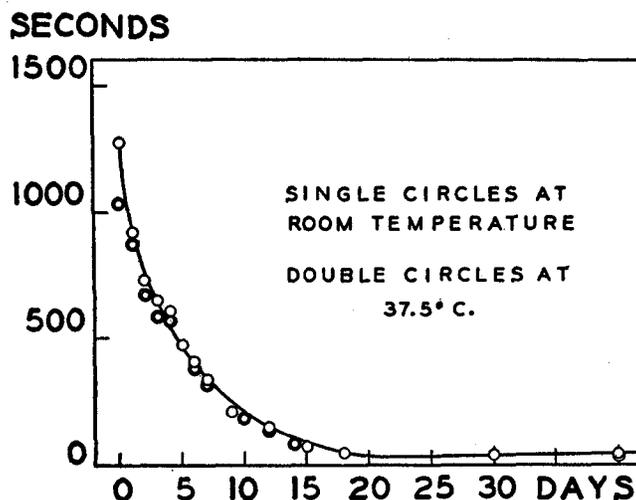


FIG. 1. The duration of spinal reflexes (ordinate) in spinal mice of various ages (abscissa).

The assumption that the decrease in resistance of growing organisms to conditions which involve a partial or complete deprivation of oxygen (such as asphyxiation by carbon monoxide, illuminating gas, nitrogen, drowning, spinalization) is due to a decrease in the faculty of partial anaerobiosis with age, seems to offer a logical explanation of our results. The literature affords abundant evidence in support of this view.

The behavior of spinal animals has been studied extensively (Sherrington, 1906; Marshall Hall, 1850; Eckhard, 1881; Owsjannikow, 1874; Eckhard, 1881; Pike, 1909; *et al.*). Most of these papers are of little interest in this connection as the

chief emphasis is put on the phenomenon of shock, while we are concerned with the gradual paralysis of the spinal cord after recovery from the shock. Sherrington has noted that the activity of the spinal cord is the better controlled the higher the animal's position in phylogeny. Babák (1907) found that in larval frogs transection of the spinal cord produces no shock. Pike (1909) has reviewed briefly the evidence for the theories of spinal shock and their applicability in phylogeny and ontogeny. The chief interest is found in several papers dealing with the stopping of the blood supply to definite regions of the central nervous system, producing asphyxia and consequent paralysis. Stenson (1667) clamped the abdominal aorta of a rabbit to interrupt the blood supply to the lumbar region and observed paralysis of the hind legs. Further references are given in Pike's paper (1909). Evidence that we are dealing with a decline of partial anaerobiosis in growing organisms is supplied by Wind (1926) and Burrows (1925) who showed that fibroblasts from the heart tissue of a 5 day old chick grew in nitrogen containing only traces of oxygen, while growth was absent in tissue from 10 day old chickens. Negelein (1925) showed that in the rat embryo the rate of glycolysis under anaerobic conditions was inversely proportional to age. Amerling (1908) found that in *Fugo* and *Rana* the resistance to O₂ lack decreases with age, and Kawajiri (1925) showed that the same conditions hold true for the Japanese salmon *Oncorhynchus mason*.

If it is granted that the paralysis of the spinal cord in decapitated mice is due to the failure of blood supply and consequent asphyxia of the nervous elements, it is highly probable that the observed differences in the periods of reflex activity between old and young animals are due to the power of young animals to exist in part under anaerobic conditions and that this faculty declines with increasing age.

SUMMARY

In spinal mice the latent period between decapitation and the disappearance of all spinal reflexes decreases regularly with increasing age (Fig. 1). Available evidence indicates that this latent period may be proportional to the capacity for anaerobic metabolism at various ages.

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