ON THE EFFECT OF COMPLETE ANEMIA OF THE CENTRAL NERVOUS SYSTEM IN DOGS RESUSCITATED AFTER RELATIVE DEATH.[1]

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Experimental studies on the effect of anemia on the brain and spinal cord are recorded as early as 1667, and are numerous, particularly of late years. Analyses of the various results obtained are given by Hayem and Barrier[2] up to 1887, and by Hill[3] and by Battelli[4] up to 1900. Reference to preceding work is also made by Prus[5] and by D'Halluin.[6] No further review, therefore, seems necessary. The latest and most valuable contributions are those of Stewart and his collaborators, Guthrie, Burns, and Pike,[7] to which, as well as to certain of the results of others, reference will be made later.

The method employed by the majority of investigators has been occlusion, either of the cerebral vessels or of the aorta at various levels. The objection to this method, which is frankly acknowl-

[1] The present article is the sequel of that on the Technique of Resuscitation, published in this Journal, Volume viii, 1906, but unfortunately circumstances incident to the severance of our former relations before its completion prevented an earlier presentation. Received for publication June 27, 1908.

[2] Hayem and Barrier, *Arch. de physiol. norm. et path.*, 1887, x, Series 3, 1.

[3] Hill, *Philos. Transactions of the Royal Society*, 1900, cxciii, 121.

[4] Battelli, *Compt. rend. de l'Acad. des Sciences*, 1900, cxxx, 800; *Jour. de physiol. et path. gén.*, 1900, ii, 443.

[5] Prus, *Wiener klin. Woch.*, 1900, xiii, 451, 482; *Arch. de méd. exper. et d'anat. path.*, 1901, xiii, 352.

[6] D'Halluim, *Compt. rend. de la Soc. de Biologie*, 1905, II, 370; *Presse méd.*, 1904, xii, 345; Thesis, Lille.

[7] Stewart, Guthrie, Burns, and Pike, *Jour. of Exper. Med.*, 1906, viii, 289; Guthrie, Pike, and Stewart, *Am. Jour. of Physiol.*, 1906, xvii, 344; Stewart and Pike, *ibid.*, 1907, xix, 328, xx, 61; Stewart, *ibid.*, 1907, xx, 407; Pike, Guthrie, and Stewart, *ibid.*, 1907, xxi, 359; Stewart, Guthrie, Burns, and Pike, *Jour. of Exper. Med.*, 1908, x, 371. (The last article contains a résumé of the literature on resuscitation.)

edged, is that the factor of collateral circulation cannot be entirely eliminated, even in the most favorable animal, the cat. Further, either the brain or the spinal cord has been separately investigated, which must make a vast difference, not from the side of determining the relative viability of the various centers, but in fixing the limit of anemia admitting of a complete recovery of the animal. Stewart[8] says, "Division of the cord in the upper dorsal region (III to VI dorsal vertebræ), if done before fairly complete recovery of the cerebral centers, is followed by collapse, dilatation of the pupil, cessation of respiration, cardiac failure and death. The integrity of the spinal centers is necessary for the resuscitation of the cerebral centers."

Other methods of investigation employed, such as artificial circulation through the decapitated head, and the introduction of emboli, preclude the possibility of recovery studies. Within the last decade, with the more or less successful attempts at resuscitation of the heart which has been made to stop beating, contributions to the subject of anemia of the whole central nervous system incidental to this state of relative death and its bearing on the possibility of general systemic recovery have been made by several observers, notably Prus and Battelli. Given a successful method for restoring to its normal functional activity a heart which is quiescent but viable, while not only interesting as an isolated phenomenon, but also promising fruitfulness in adding to our store of information, its main value is not absolute but dependent upon the power of resisting the malign effects of the cessation of the circulation possessed by the other organs and tissues. That the nervous system naturally comes first in the consideration of such a relation needs no discussion.

This study of brain anemia was the sequence of our work on the resuscitation of animals killed by anesthetics and asphyxia,[9] which may be briefly summarized as follows for the purpose of this paper. By means of a centripetal arterial infusion of salt solution under sufficient pressure, together with the injection of one to two cubic centimeters of 1–1,000 adrenalin chloride in mass

[8] Stewart, Guthrie, Burns, and Pike, *Jour. of Exper. Med.*, 1906, viii, 389.
[9] Crile and Dolley, *Jour. of Exper. Med.*, 1906, viii, 713.

dose early and along with the infusion, and the simultaneous employment of vigorous artificial respiration and gentle but firm cardiac massage through the unopened thorax, a heart which has ceased to beat may be excited to resume beating within certain limits. Up to five minutes of total cessation of function these efforts are uniformly and readily successful, provided that the full technique has been used; up to ten minutes, there is an occasional failure, but after that the chances of success become progressively less, and our limit was thirty-five minutes in puppies (three cases). While it is true that this method in our hands was not efficacious in resuscitating a quiescent heart after a longer interval, which result has been attained by prolonged direct massage (*e. g.*, after one hour, by Prus), nevertheless, it is uniformly successful within the limits which are compatible with viability of nervous tissue, both according to our own results and the consensus of opinion of later writers. The method is necessarily self-limited, for in the case of a heart which is losing its irritability owing to lapse of time, dilatation occurs from the infusion before the requisite amount of stimulation is given, and as maintenance of pressure in the coronary arteries is the most essential factor, the infusion must be continuous. Indirect massage of the heart by compression of the chest, while generally viewed as insufficient, is a subsidiary factor, and has proved satisfactory, even in dogs with rigid chest walls. In periods under five minutes, hardly any is necessary. In no case in our experience has clotting in the heart been an obstacle without concomitant and unnecessary cardiac trauma.

Our purpose being primarily to determine the period of anemia the central nervous system could stand with subsequent recovery, the method offers the advantage that no operative procedure is necessary except the small incision for inserting the infusion cannula. Our results are based, first on a series of thirty unselected dogs, resuscitated after various times, in all but five of which the subsequent course of events was not disturbed. These five were killed after different times for the purpose of histologic examination. Secondly, the series of sixty dogs, previously reported in the paper on resuscitation, was drawn upon for data pertaining to this work. In the latter experiments blood-pressure and respiratory tracings were made.

TECHNIQUE.

For the recovery experiments, with one exception, the dogs were killed by chloroform. While open to objection on account of the paralyzing effect on the nervous system, and the non-elimination until after the resuscitation, this method was adopted in imitation of the condition most likely to afford opportunity for resuscitative measures within the time limits of successful application, *i. e.,* respiratory and cardiac failure in the course of surgical operations. All procedures were done with the customary aseptic precautions. Ether was used for preparation, and the infusion cannula was inserted in the axillary artery, thus saving the cerebral vessels. In the majority of cases ten minutes under ether sufficed, in a few fifteen were necessary, and exceptionally, somewhat longer. As little ether as possible was given and the dog was allowed to come well out of its influence before starting the chloroform. This was usually administered from a well-ventilated cone, though sometimes through the throat tube. The latter method was employed when this tube for future artificial respiration was applied before respiratory failure. The throat tube, which was tried to obviate the necessity of an operation for a tracheal cannula, proved most satisfactory, and would doubtless be equally efficacious for the human subject. It is bent to conform to the oral cavity, with one end somewhat pointed and with a small flange one inch therefrom to catch behind the vocal cords.

In order to estimate in some measure the effect of the amount of anesthesia on the subsequent course of the dogs, two experiments were made of anesthetizing the dog in the usual way to the point of respiratory failure and resuscitating it by artificial respiration without permitting cessation of the circulation. The first dog showed full return to intelligence in sixteen minutes. The second one took ether like an alcoholic, and it was forced for ten minutes before struggling ceased. However, in twenty minutes after recurrence of the respiration the animal walked about and showed return of functions, though extremely groggy.

The period of total anemia was estimated to start from the moment when the first heart sound ceased to be audible with the stethoscope, this sound sometimes persisting for several minutes

after the failure of blood-pressure and the disappearance of the carotid or femoral pulse and the second sound. While this is only the statement of the well-known fact, attention is called to it because very possibly in some experiments it makes our stated period of anemia shorter than it actually was, with a circulation too feeble to reach the brain. In some cases, with the heart sounds becoming fainter and fainter, it was impossible to record the actual moment of failure. In these a leeway of at least one-half minute was allowed from the last distinct sound to the recorded cessation. From the time of starting the chloroform to respiratory failure there was an average of two and three-fourths minutes, with a minimum of fifteen seconds and a maximum of seven and one-twelfth minutes (Table I). The stoppage of respiration and the final failure of the heart were synchronous in five cases, from which the intervening time varied up to six and three-fourths minutes, with an average of one minute and fifty-seven seconds. From a study of the tracings of the first series it was found that the blood-pressure was at the base line during an average time greater than the latter half of this period. It is probable, therefore, that during this period the cerebral circulation was reduced nearly to the vanishing point, and while a small amount of blood goes a long way in the brain, Leonard Hill saying, "It is obvious that the cortex can be kept from death for hours by the merest dribble of blood," this marked anemia of several minutes duration had an effect which was apparent in that the cases with prolonged partial anemia did not recover to the same degree as the average dog subjected to total anemia of the same duration. It is worthy of note that in the dog of maximum recovery, which was one and one-third minutes above the time of the second best result, only twenty-two seconds intervened between respiratory and cardiac failure.

In five out of the twenty-nine animals killed by chloroform, there was a brief spontaneous recurrence of the heart sounds, occurring from twenty seconds to one and one-half minutes after they had entirely ceased, and accompanied in two by two or three faint respiratory efforts. In only one was the carotid pulse palpable. As their total time cannot be exactly classified, both their absolute and practical times will be given.

The time spent in resuscitation is included in the period of total anemia. While it seems reasonable to suppose that a centripetal arterial infusion of salt solution aided by indirect massage of the heart would hardly reach the brain to any extent during a period of administration of from one to three minutes, and, further, from the consideration that if it did, there would be very little blood in the salt solution, the question was put to the test of experiment. In a dog dead for twelve minutes, a solution of methylene blue was infused into the axillary artery, and the usual procedures, with the exception of adrenalin injection, were carried out for double the average time. No indication of its having reached even the bulbar centers was found. This is in contradistinction to direct massage, which effects a veritable artificial circulation, according to D'Halluin, sufficient to reanimate and maintain bulbar activity. Study of the tables of Prus shows that by direct massage respiration returned in twenty-nine out of thirty-five experiments in one series, though there was no return of effective heart beat, and in seven cases, reflexes and muscular movements reappeared.

The definition of the end of the period of total cessation of the circulation was, however, sharp, the resumption of function on the part of the heart being abrupt, visible as well as palpable. After a few initial sounds blood pressure rose rapidly, often within ten seconds, to as much as 200 mm. Hg or over, due to the adrenalin effect.

RESULTS IN RECOVERY (Tables I and II, p. 807).

Permanent and complete recovery was obtained after five minutes, six minutes,[10] six minutes and ten seconds, six minutes and fifteen seconds,[11] and seven minutes and thirty seconds of total cessation of the circulation. That is, one dog out of twelve with total cessation of circulation between the periods of seven minutes and eight and one-half minutes recovered, whereas only one out of seven between the periods of five minutes and six and one-half

[10] Recurrence of heart sounds interjected for thirty seconds; practical time six minutes and thirty seconds.

[11] Recurrence of heart sounds for one minute and twenty seconds; practical time six minutes and thirty-five seconds.

minutes died apparently as a direct result of the anemia. Complete recovery was presumptive in another dog after seven minutes and thirty seconds. This was an early animal of the first series when technique was the object in view; it was killed on the second day on account of suppuration around the tracheal cannula. He was walking around in good general condition, though no specific examination was made. One dog of the second series, after five minutes and thirty seconds, was killed after twenty-four hours for the purpose of histological examination. Compared with the others of the same degree his condition assured a probable recovery. The asphyxiated dog, five minutes and forty-five seconds in time, was killed on the fourth day on account of a gangrenous inflammation of the axillary wound. A second animal of the first series, seven minutes in time, was killed on the third day since he appeared moribund. He was found to have thrombosis of both sides of the heart, with clots extending into the arteries—a sequel of violent massage. Excluding these accidents, the recovery of the last two animals would have been probable, since no dog that died lived longer than thirty-six hours, in all but two death occurring under twenty-four. Our experience shows no intermediate condition of fatal outcome delayed for several days uncomplicated by accidental organic lesion, in other words, no slow decline to death. The demarcation between recovery and death is a sharp one. The crisis in practically all the experiments was reached in from twelve to twenty-four hours. Then death quickly ensued or distinct improvement of nervous functions shortly began, continuing more or less rapidly until complete restoration, though the convalescent period lasted in two dogs four and six weeks respectively.

From his studies on the effect of different degrees of anemia by means of occlusions, Leonard Hill says: "The degree of anemia required to produce dementia is separated by the narrowest line from that which produces coma and death of the respiratory center. There are either no symptoms or death in a few hours." Our results accord with this statement. Up to a certain point, not to be exactly limited, but roughly six minutes, the after-effects are not marked and the second, third, or fourth day brings com-

plete recovery. For example, one dog (Experiment 10), after four minutes and ten seconds, showed entire return of intelligence under one hour, evinced partly in well-defined efforts to escape from the laboratory, while another after six minutes and ten seconds (Experiment 29) showed general return of function within twenty-four hours. Beyond the six-minute limit, however, there is a great deal of after-effect, increasing out of all proportion to the increase in the duration of the period of anemia, reaching as well in the dogs which finally recover a temporary state in which the animal is little more than a cardio-respiratory mechanism, and beyond this limit recovery is altogether uncertain, but if the stage of depression is tided over, recovery has been eventually complete in our experiments, though the narrowness of the escape is indicated by the degeneration of a certain number of neurons in the recovered dogs whose brains were studied by the Marchi method. This does not exclude the possibility of a partial recovery in the sense of a permanent localized after-effect, such as the paralysis of one fore leg described by Stewart[12] in two animals which, however, were under observation only seven and nine days, respectively. In our dog with recovery after anemia of maximum duration, it was the pyramidal fasciculus in which the degeneration predominated. The distinction here has reference to the ability of the whole organism to maintain life at all. The viability of the vital centers, as well as other centers, is considerably above that of the brain as a whole, as the results in recovery prove, and the immediate outcome must depend on the maintenance of the inter-relation and association of all centers, cortical and subcortical. Stewart[13] says that, when exposed to adverse influences, the synapse proves the weak link in the nervous chain.

In general the following sequence of return of the various functions and reflexes was exhibited: respiration, vasomotor control, corneal reflex and knee jerk (tendon reflexes in general), winking, cutaneous reflexes, partial or complete contraction of pupils and light reflex. This order was subject to considerable variation, which will be considered under the special discussion of func-

[12] Stewart, Guthrie, Burns and Pike, *Jour. of Exper. Med.*, 1906, viii, 289.
[13] Stewart and Pike, *Amer. Jour. of Physiol.*, 1907, xix, 3, 328.

tions and reflexes. Hypertonicity of the voluntary musculature immediately succeeded recovery of a normal tone and was manifested by exaggeration of the knee-jerks if not by a more or less widespread spastic condition. It always followed rapidly the reappearance of the knee-jerk. Reflex muscular movements, secondary to skin or tendon stimulation, always preceded those of spontaneous origin. Spontaneous incoördinate movements appeared sometimes before, sometimes after the light reflex, but afterward only when the light reflex returned relatively early. Incoordinate movements followed quickly in the dogs with anemia of short duration, so that perhaps the incoördinate movements did not appear, but the resumption of muscular activity was sudden, the dog starting up as though suddenly aroused from sleep. Succeeding the coördinate movements were what may be classed as purposeful movements, involving all the muscles of locomotion and being attempts to turn over, to arise, or to crawl forward. Usually after the appearance of coördinate movements, less frequently about the same time, visual and auditory reactions were obtained. The auditory was always the more definite, and usually returned first. It is the combination of the return of the special senses with purposeful muscle movements, all together or in part, that is termed consciousness, though it has been usually very dim and uncertain. In many of the dogs which succumbed after some hours there was more than a mere reflex revival, there being some manifestation of the higher faculties in addition.

The course of events following the resuscitation may be summarized as follows: A state of hyperexcitability follows reanimation, reaching its maximum in one to three hours, when retrogression begins. This second stage is characterized by the onset of uncontrolled muscular movements, either coördinate or convulsive, lasts a longer time, and gradually passes into the third stage of depression and paralysis, in which the reflexes are more or less involved. The dogs which recovered from this never exhibited as much mentality nor such an activity of reflexes on the second day as for a short time after the resuscitation. Consequently, it is our opinion that the extent of temporary recovery in the dogs which died was merely a manifestation of the first stage of hyperexcitability.

The average picture toward the end of the first stage, for a recovery dog, is one of an animal in a very stuporous condition, for the most part lying quietly, with an accelerated pulse and much quickened respiration, expiration being prolonged and more labored, with normal conjunctival reflexes, with cutaneous reflexes constantly present in the paw stimulated but less so in the homolateral fore-limb, and least so in the contralateral hind-limb, with exaggerated tendon reflexes, and with pupil reflexes, if present, uneven and tardy. There is a general spastic condition of the muscles, the legs being commonly held in extension. On loud sounds in close proximity, the head may be raised, the eyelids opened with dilating pupils, and the ears pricked up, the attitude being simply one of attention without localization or indication of ideation. To a flash of light, the head may be withdrawn, but usually there is only a lid reflex. Especially on disturbance but sometimes without it, the animal arouses, barks, looks around, and exhibits coördinate and even purposeful and propulsive movements of the legs and body, attempting to rise or to crawl, usually unsuccessfully, but at times succeeding in getting to the standing posture or in a short progression, lasting a few moments, depending on the extent of the paralysis, and then falling at once into stupor.

The second stage, of retrogression, was a constant phenomenon in all the dogs but was much less marked after the shorter times. The animal becomes progressively more comatose, the spastic condition, which had largely disappeared with the reanimation, returns, visual and auditory reaction disappear, and the skin reflexes become inconstant. Muscular movements, however, are kept up, but are less coördinate and more spasmodic. This seems to depend on the duration of the anemia, convulsive movements being little marked after the shorter times. On the other hand, the dog with recovery from anemia of maximum duration had definite tono-clonic convulsions. When such convulsive movements are well marked, after a period of hours the animal passes into a deep coma, with a general condition from which recovery hardly seems possible. This lasts well into the night, but the second morning finds a distinct improvement.

Up to this point, the course of events in the animals which

succumbed, embracing all but one with anemia over the seven-minute period, while limited according to the extent of the recovery, was similar to that in the dogs which did eventually recover. In the usual sequence, a few did not attain a light reflex and the majority came back so far as to exhibit coördinate movements and auditory reaction, but only in two was there apparently dim consciousness. Reanimation of the higher faculties was much more transient so far as it occurred, and the animal passed more quickly into coma from which it was impossible to arouse. Irritability of the muscular control was much more marked, with a few exceptions, periods of violent convulsive movements alternating with periods of quiet and stupor. While these muscular movements were partly clonic and tono-clonic in character, commonly an element of coördination was maintained, and they were distinctly propulsive and progressive, though violent and uncontrolled.

Of the coördinate movements, the running motion of the legs such as is frequently seen in the early stage of anesthesia was the best example, and was performed with extreme rapidity, the dog lying partly upon its back with its legs waving rhythmically in the air. Sometimes only the fore-legs were involved, but usually the movement was general. If the dog was not so completely paralyzed, this resulted in a crab-like progression about the room. The strictly convulsive movements were very complex, clonic and tonic types being mingled, with a violent threshing about. In several instances there was some opisthotonus. The slightest disturbance provoked the movements characteristic for the animal.

The quiet periods in the early stages were of short duration, but the interval was distinct. In the later stages, they became more and more prolonged. Finally, as if worn out, quiet would ensue, the animal being perfectly limp, tendon and skin reflexes first disappearing, next the eye reflexes, leaving only the cardio-respiratory functions, with respiratory failure not far off.

To show the slow return of faculties and the paralyzing effect of the maximum period of anemia from which recovery was made (seven minutes and thirty seconds in Experiment 27), the subsequent course of the dog in this experiment will be given in some detail. On the second day she was awake but paid no attention to

her surroundings. To loud sounds there was only an occasional response and blindness appeared absolute. The hind legs were entirely paralyzed, but when the hind quarters were supported she was able to walk on the fore-legs, though the progression was cross-legged or spraddling. Sensation was much more deficient than motion, no attention being paid to prolonged immersion of any foot in cold water. A strong bull-dog clamp on a hind paw was not noticed beyond restlessness, though on a fore-paw it was vaguely localized after several minutes, but only to the extent of a reflex from the leg itself, and there was no coördinate attempt at removal. Food was not recognized when placed in the mouth and was held there passively. No notice was taken of tobacco smoke or ether fumes. The third day she walked about, though unsteadily and with a decided stringhalt gait of the hind-legs. Water was recognized after standing in it for several minutes. The legs gave way when she jumped off a chair. Hearing was very acute but vision appeared to go no farther than mere perception of light. Localization of sensation by the clamp test was improved to the extent of biting rather aimlessly and very incoördinately at the foot affected, very frequently the wrong leg being attacked if in juxtaposition. It was not until the seventh day that the clamp was recognized, grasped and pulled off. On the third day also the feet were withdrawn from cold water, but the sense of position was not evident till the fourth day, tested by resting the feet on boards at different levels. Only maximum differences of level were then recognized. While the animal appeared hungry, constantly licking her chops, food was not recognized until the fifth day. It was after a week that tobacco smoke and ether fumes were noticed.

While in a week's time the return of all faculties with the exception of vision was indicated to a greater or less degree, the animal was by no means normal but exhibited great hebetude in all respects. She was very lethargic, would not run nor play, and response to any stimulus was delayed and feeble. How much of this was due to the blindness, it was impossible to say, but certainly not all. For two weeks there was hardly perceptible improvement in vision. She paid no attention to attempts at testing it and when she moved about it was slowly, feeling her way, though about

the end of this time she would notice moving objects within a range of a foot or two, with distinctly more accuracy when they were held above the level of her eyes. From this time improvement steadily continued and in four weeks recovery of vision was complete. With recovery of vision the condition of dementia entirely disappeared, and not till then did the psychical faculties of fear, pleasure, and memory become normally evident.

A summary of the extent of temporary reanimation in the dogs which succumbed at such a time as to permit sufficiently exact observation is arranged in the sequence before given as follows: Of seven dogs with anemia ranging from five to seven minutes, one died after twenty-four hours. If he returned to consciousness at all, the return was exceptionally tardy as compared with that of the others with the same period of anemia. Of those dying after periods of seven to eight minutes, two revived as far as spontaneous coordinate muscular movements, without visual or auditory reaction or return to consciousness, while one failed of vision. Of five after eight-minute to nine-minute periods, one did not show even the light reflex and much less did it come out of coma; two recovered to the extent of muscular movements, a fourth added auditory reaction, while in only one was there a suggestion of a return to consciousness. Of three, after nine-minute to ten-minute periods, one went as far as apparent consciousness, one failed at vision, and the third showed nothing beyond the light reflex. One dog at twelve minutes and ten seconds gave only a reflex revival, and in the dog of the recovery series with the longest period of anemia only coördinate muscle movements appeared in addition.

SPECIAL PHENOMENA FOLLOWING RESUSCITATION.

Respiration.—(Table III.) Respiration has recurred in every animal in which the circulation was restored and maintained sufficiently long. The maximum case, thirty-two minutes of total anemia, gave respiratory recovery twenty-one minutes after circulatory to the extent of three faint gasps, but cardiac failure immediately ensued. Comparison of the time of restoration of respiration in our experiments with that recorded by several other observers gives an interesting result, *i. e.*, a much more rapid re-

covery. For our experiments, the average time for restoration for animals between the periods of three and eight minutes of total anemia was three minutes and fourteen seconds. The average time after occlusion of vessels in Stewart's cats and dogs between the same periods was seven minutes and forty-one seconds; for Prus' chloroform series with periods between three and five and one-half minutes was seven minutes and nineteen seconds (with frequent return of respiration before efficient heart beat). Battelli's successful chloroform cases of the same time are too few for comparison, but in general both these and the electrocuted dogs concord with the above results. Hill[14] says that a certain arterial pressure is necessary to invoke respiration. This comparison points to the increased effectiveness of the higher pressure due to adrenalin.

The first gasp was distinct and fairly strong. After a few gasps, in the majority of the animals, inspiration came to exhibit a triple character, with the inspiratory-expiratory ratio three to one, such as occurs in sobbing. This lasted for several minutes. Gradually the rate increased and the rhythm became regular. A sudden assumption of the normal type of breathing sometimes happened in the dogs with short time of anemia and was always associated with simultaneous recovery of the eye reflexes. A rapid increase of rate was the rule in all cases, as much as 100 per minute being recorded, but usually the high rate did not continue for long. For example, it was 72 per minute sixteen minutes after resuscitation in the dog which recovered after anemia of seven and one-half minutes and fell to 36 in about twenty minutes. Afterward it was subject to frequent changes, and not till the third day was a normal rate established in some cases. When the rate slowed, a prolonged and labored expiration was characteristic. The changes of rate in the initial respirations will be best illustrated by reference to the protocols of two experiments.

EXPERIMENT 27.—Hound puppy, about eight months old. Seven and one half minutes total cessation of the circulation.

11.45.30. Return of pulse suddenly appearing in the tongue is first noticed.

11.47.30. First respiration. The first four respirations occur at thirty second intervals (4 per minute) and then for about three minutes at seven second

[14] Hill, The Physiology and Pathology of the Cerebral Circulation, London, 1896, p. 132.

intervals, the inspiratory portion comprising three distinct efforts in all. Fibrillary contractions of the tongue occur after beginning of respiration.

11.55.00. Lachrymal secretion begins. The right pupil is distinctly contracted.

11.58.00. Respirations rather suddenly assume normal character and rhythm with rate of 24.

12.00.00. Respiratory rate has jumped to 48. (Noted further above.)

EXPERIMENT 30. One year old puppy. Twelve minutes and ten seconds total cessation of circulation.

11.30.15. Heart beats, recording from first observation of the pulse in the axillary cannula. Though the infusion tube is partly clamped by the finger, pressure is sufficient to drive the blood into the infusion bottle at a height of five feet.

11.32.25. First respiration occurs. The movement and those following for several minutes are deep and gasping. For four minutes the rate is very irregular, at intervals varying from five seconds to one minute. Artificial respiration is kept up continuously during this time but is stopped as soon as spontaneous respirations become more regular.

11.37.00. Respirations now occur at three to five second intervals.

11.38.00. Respiratory rhythm is more steady (20 per minute) and movements more shallow.

11.44.22. Respirations, 28 per minute.

12.00.00. Respirations, 32 per minute, are somewhat more irregular and spasmodic. Expiration is distinctly labored.

12.13.00. Respirations, 40.

12.40.00. Resprations, 32. The dog is evidently failing, and about one hour later is found dead.

Blood Pressure.—(Table III.) The use of adrenalin complicates the study of the blood pressure changes. In a successful resuscitation, as already noted, the blood pressure rose rapidly, often within ten seconds, usually to a height of 200 mm. of Hg and in one case, 250 mm. This level was maintained from two to five minutes in all but the dog with 250 mm. of pressure, and then it began to fall as the effect of adrenalin was dissipated. From ten to forty minutes elapsed before the lowest level was reached. Depending on the extent of the vasomotor reactivation, either a tendency to rise was immediately exhibited or the low level persisted for from ten to twenty minutes, in the latter case with a subsequent rise. In two animals, after total anemic periods of seven minutes and thirty seconds and eight minutes and thirty seconds, one of which at least may be credited with presumptive recovery, this second level was maintained until the animals were killed—in twenty-four hours and in five and two-thirds hours respectively—but in the others, all

with anemia of longer duration, it was only a temporary reanimation, and along with the reflexes, steadily declined to death.

On account of the effect of adrenalin overlapping the return of vasomotor activity, particularly after the shorter periods of anemia, the relative time of the reactivation of the center could not be absolutely determined. Stimulation of the sciatic nerve did not cause the usual rise of pressure until the secondary rise before mentioned had begun, and respirations were well established before this rise (see Table IV). In fact, with the exception of one experiment in which respiratory recovery was synchronous with the first successful stimulation test obtained shortly before a manifest rise, respiration in all experiments had returned well before the end of the first fall. In one experiment of the second series, as little adrenalin as possible was used. The anemia lasted five and one-half minutes (two-minute recurrence of heart), and respiration began in two minutes after restoration, while reaction to sciatic stimulation was not obtained for four minutes. Synchronously with it, respiration rather suddenly assumed a more normal type. It appears, therefore, that the return of the vasomotor center is nearly synchronous with respiration after the shorter times of anemia, but is more delayed after the longer times. In the puppies after thirty-five minutes there was apparently no vasomotor reactivation.

Reflexes.—(Table IV.) While varying considerably in the time of their recurrence, after the same amount of anemia, the corneal reflex and spontaneous winking returned in all but the three experiments which did not proceed sufficiently long. Up to eight minutes the light reflex reappeared constantly, though it was the least uniform in time and degree. After eight minutes it was inconstant. The maximum time after which the corneal reflex reappeared was twenty-four minutes (maximum resuscitation in adult dogs), and for the light reflex the maximum time was fourteen and one-half minutes.

The knee-jerk varied the least in its range. It was also noted in the maximum resuscitation. Not infrequently there was a difference in the time of recurrence of the bilateral reflexes, in two cases one corneal reappearing three minutes before the other, though for the knee-jerk no difference over one-half minute was noted.

As to the relative time of the reappearance of reflexes, first place belonged to the knee-jerk more frequently than to the corneal reflex, though they were synchronous four times. The corneal reflex always preceded spontaneous winking while in every case the cutaneous reflexes returned before the light reflex.

Temperature.—While not recorded as a routine, sufficient data have been obtained to indicate that the temperature continues to fall for several hours following the resuscitation. The lowest temperature per rectum was 32.9° C. four hours after anemia of nine and one fourth minutes (Experiment 1), and 33.8° C. was reached in sixteen minutes after thirteen and one-third minutes of anemia (Experiment 5). From this point the temperature gradually rose to a state of hyperpyrexia, which was more marked in the animals which succumbed. In the dog which recovered after the maximum period of anemia the maintained level was reached the second day.

Phonation.—Nine and one-quarter minutes (Experiment 1), was the maximum after which this faculty returned. Actual barking, indeed, occurred in but one other case over seven and one-half minutes (Experiment 14), though there was whining or imperfect attempt at vocalization in three. Phonation usually appeared synchronously with or shortly after the exhibition of spontaneous muscular movements, that is, one-half to one hour after resuscitations following anemia of about seven minutes.

Micturition or Defecation.—Micturition or defecation occurred in the majority of animals during the period of hyperexcitability.

Auditory, Visual, and Olfactory Senses.—As already indicated, the reaction to auditory stimuli was definite and unmistakable during the period of hyperexcitability in the recovered dogs, while to various visual stimuli during the same time, the only response was a lid or pupil reflex, but out of fifteen animals with anemia of duration including and over seven minutes, only six gave even a temporary recovery of hearing. Further, in the animals which recovered, the later effects on vision were much more marked, in general increasing as the limit of recovery was approached. For example, in the dog with recovery after maximum anemia, hearing was reasonably acute on the third day, though vision was not fully restored for three weeks, while in the animal with anemia of six and

one-sixth minutes (Experiment 29), the best example of early visual recovery, hearing was normal on the second day, though a day more was required before the animal ran about without collision with obstacles. The maximum period after which hearing was observed was nine and three-fourths minutes (Experiment 15). The sense of smell came back between hearing and vision, though the test was never definite unless irritating fumes were employed. The first reaction to these was on the third and seventh days, respectively, in dogs with anemia of six and seven and one-half minutes (Experiments 2 and 27).

Phenomena Referable to the Cortex.—Most of the animals which recovered passed through a final stage comparable in many respects to the condition of Goltz's[15] decerebrates; such a period was characterized by dementia and loss of intelligence, the lack of any psychic response to stimuli, and the inability to recognize food and drink. Response to stimulation was purely reflex, or absent if memory of past experiences was involved; for example, meat placed in the mouth was held there passively or in one case forcibly spat out, a flash of light was answered by a lid reflex, and there was indifference to the relative position of the fore-legs. Power to localize stimuli was of gradual acquirement. Restlessness, however, was generally not observed.

That the temporary paralysis was of cortical origin was indicated by the associated exaggeration of the knee-jerks. The motor function did not suffer as much as the sensory, for the paralysis disappeared distinctly before the return of intelligent and normal response to stimulation. The clinical observation that the cortex suffered the most and was the last to recover is supported by the fact that the histological alterations were more marked in the cortex than in the lower centers.

THE HISTOLOGY OF FATAL ANEMIA AND OF ANEMIA WITH RECOVERY.

Nissl's Method.—The neurocytes stained by Nissl's method were studied in ten cases, as follows: after short periods of anemia with rapid general functional recovery, the brain being removed one

[15] Howell, Text-book of Physiology, Philadelphia, 1905; and Schäfer, Text-book of Physiology, Edinburgh, 1898–1900.

hour after resuscitation (Experiments 10 and 12); in one case of most probable eventual recovery, twenty-four hours after the resuscitation (Experiment 8); in one case well beyond the limit of probable recovery, one and one-third hours after the resuscitation (Experiment 9); and in six animals which died (Experiments 1, 5, 7, 14, 15 and 16). In several of the fatal cases the brain was removed immediately after death, and in all the others the material was obtained before or almost before the heart's beat had ceased. In all cases, sections were made from the different parts of the central nervous system from the cord to the cortex. The tissue was fixed in 96 per cent. alcohol, and for cutting fastened to the blocks with celloidin without imbedding. The alterations described are based entirely upon a comparison with three control animals subjected to the same amount of anesthesia, in which the stainable substance was as a whole uniform and well defined. Only the motor stichochrome cells were considered, though frequently the changes were so marked that they could be diagnosed only by their size and relations. In studying the preparations comparatively, the plan was adopted of making differential counts of a fixed number of cells, the changes being classified into slight, moderate and marked, and tabulating them.

The effect of anemia has been previously described by Mott,[16] who used the materials from Hill's experiments on occlusion, and by Sarbo[17] and Marinesco.[18] The present work confirms their observations; briefly, the changes, where slight, consist in a swelling of the tigroid masses, where more marked, in partial or complete disintegration, either into smaller granules or into fine dust-like particles with a diffuse staining of the cell. The periphery of the cell with its processes suffers more.

The results of the comparative study were as follows. The alterations in the same case showed a progressive increase in severity from the cord and medulla to the cortex. The fatal cases uniformly presented the greatest change, not merely chromolytic, but here and there definitely indicative of cell death. Nuclear stains were also employed, and brought out what the Nissl method

[16] Mott, The Croonian Lectures, 1900.
[17] Sarbo, *Neurol. Cent.*, 1894, xix, 664.
[18] Marinesco, *Presse med.*, 1897, v, 41.

had suggested, namely, the frequency of structural alterations in the cells. In the mildest form only a swollen condition of the whole cell was visible. Serious involvement of the nuclei was manifest frequently in their eccentric position or even in their disappearance. With slighter injury, possibly no nuclear membrane appeared, though the nucleolus remained intact. In fact, the nucleolus seemed to be the most resistant element. Other appearances occurring alone or associated with the preceding were an apparent diminution or an irregular massing of the nuclear material and occasional vacuolation. The marked changes were practically confined to the fatal cases. These findings, supported as they are by evidence of degeneration of fibers, place the limits of experimental resuscitation upon an anatomical basis.

Of the two dogs with rapid functional recovery, one (Experiment 12) after three minutes of anemia matched very closely the controls, but in the other, four and one-sixth minutes, the tigroid substance stained poorly. While it is true that for the time that had elapsed the animal had progressed well toward recovery, and the technique may have been at fault, the experiment suggests an explanation for the two deaths (Dog 17 and Dog 23) which occurred under the usual limit. Dog 17 after the same period of anemia died from respiratory failure in fifty-three minutes, after having progressed to eye reflexes, barking and muscular movements, and Dog 23, after six minutes and five seconds of anemia died twenty-four hours later, its reanimation having been comparatively imperfect. In terms of this explanation, the poor resistance in these animals may be expressed by saying that they were handicapped by a preëxisting functional derangement of their nerve cells. Further, among the fatal cases showing parallel changes, was an early death (Experiment 7 with death in forty-four minutes after seven minutes of anemia) which bears out the preceding. On the other hand, that the anemia alone was not responsible for the appearance was indicated by the animal with an anemia certainly sufficient to cause death (Experiment 9); its course was terminated shortly for examination, and therefore it is comparable as to the time after resuscitation with the last experiment but in staining it ranked next to Experiment 12 with

its rapid recovery. A comparison of this same case with the one twenty-four hours after the resuscitation (Experiment 8) gave differences in favor of the former, that is, after a fatal period of anemia examined shortly after resuscitation there was less change than after a shorter period promising recovery, examined at the end of twenty-four hours. This fact points to a progressive effect following an anemia of the character produced and is in accord with the generally expressed views as to the nature of the Nissl substance. For some time after the resuscitation the cells subsisted upon their stored-up energy. While the histological data upon this point are meager, they fit in with the stage of depression following the stage of heightened irritability uniformly observed.

Marchi Method.—(Photographs.) This method was used in four fatal cases (Experiments 16, 23, 24 and 25) and in two of the recoveries (Experiments 22 and 27). Preparations were made from the optic tract and the spinal cord and medulla and, in addition, from the pons, cerebral peduncles, and internal capsule in the dog with recovery after maximum anemia. This dog gave the most interesting findings. In the cord, with a very few blackened fibers scattered throughout the white matter, the degeneration was localized in the lateral pyramidal fasciculi and in the proper lateral fasciculi of Flechsig. This localization was more marked on the left side, and while only a relatively small proportion of the fibers were involved, it was sufficient to mark out these tracts. Of the pyramidal fasciculus, on the left side nearly one hundred, and on the right side between thirty and forty fibers were affected. In the higher sections, this fasciculus was readily traceable to the cortex by the presence of this degeneration. It is, therefore, apparent that in this animal a small proportion of the psycho-motor cells entirely succumbed to seven and one-half minutes of total anemia. Failure of the cells to recover was escaped by a narrow margin, though the dog, which was killed after one month, gave no evidence of disability. A similar finding is recorded by Mott in one of Hill's monkeys after ligation of both carotids and one vertebral; in ten days the animal had returned to a normal condition, but showed the degeneration of about sixty fibers on the side opposite the ligated vertebral artery.

The other dog which recovered also gave a picture of degeneration, but of a different character. While the actual number of fibers involved was greater, not only was there no localization but there was an early stage of degeneration with droplets of varying size, scattered in longitudinally cut spinal nerves at intervals along the course of the fibers affected. This animal, which was killed in six days was, at the time of death, partially blind and deaf, and though it could stand, it was too paralyzed to maintain the upright posture or to walk. The question arises as to whether it would have eventually recovered. Judging from the other animals which, with final recovery, passed somewhat more rapidly through a similar condition, and from the fact that there was a noticeable improvement from day to day in the animal just mentioned, general recovery, with a complete destruction of a few neurons, is probable.

An early degeneration similar to that mentioned occurred in the fatal cases, though the number of fibers involved was considerably less. None of these animals had lived over thirty-six hours at the outside. On account of the shortness of the time which had elapsed, this appearance was unexpected and will be further investigated. However, it corresponds with the organic changes in the cell-bodies which occurred during the same time.

COMPARISON WITH THE RESULTS OF OTHERS.

Mayer[19] concludes that from ten to fifteen minutes is the limit for general resuscitation, though respiration and the vaso-constrictor activity may recover after that time. Stewart,[20] with complete recoveries after occlusion of cerebral vessels for five, six, eight, nine and five-fifths, and sixteen and one-half minutes, agrees with Mayer's conclusion. Hayem[21] says that in general, brain functions are not recovered after from ten to eleven minutes. The conclusions of Batelli and of Prus are the only ones drawn from observation of animals resuscitated from apparent death. None of Battelli's dogs survived, and he ascribes this fact to the severity of the operation on the thorax necessary for his resuscitative measures of electrization and heart massage; he says that, aggravated by the violent

[19] Mayer, *Med. Cent.*, 1878, xvi, 579, 594.
[20] Stewart, Guthrie, Burns and Pike, *Jour. of Exper. Med.*, 1906, viii, 298.
[21] Hayem, *Archiv de physiol. norm. et path.*, 1888, i, Series 4, 103.

respiratory efforts, the animal passes into coma and dies. However, from the extent of reanimation exhibited, he concludes that the functions of the central nervous system may be reëstablished after ten minutes of total anemia, but not constantly after fifteen, and the maximum limit is twenty minutes. Prus does not fix a definite limit. Stewart suggests that in such prolonged periods of one and two hours as those of Prus, the auricles must have kept up a slow, but in some degree efficient, movement of the blood through the brain. On account of the injury from opening the thorax, Prus attempted recovery in only thirteen out of fifty-two dogs reanimated, the others being killed after a short time. Two of these survived. One was killed by asphyxiation, and the period of total anemia was six minutes, estimating from the stoppage of the heart to the beginning of direct massage, as considered under "Technique." From the data given, the subsequent course of this animal corresponds closely to our six-minute periods. The other was after a period of four minutes killed by chloroform. The dogs that survived from three to five days were all subjected to anemia of short duration, and of the two cases above six minutes, both ten minutes of total anemia, one died in six and one-half and the other in twenty-four hours, all the deaths being ascribed to infection.

From our experience, it seems justifiable to say that observation of an animal resuscitated from a state of completely suspended animation is very misleading unless carried far enough, and does not permit of conclusions regarding the limit of anemia admitting of recovery. For there quickly ensues a condition of hyperexcitability of reflexes, associated with voluntary movements and with greater or less return of the special senses, even with an apparent return to consciousness; consciousness is transient, but appears in animals which succumb as well as in those which eventually recover. In our experiments this phenomenon was exhibited in dogs subjected to nearly double the amount of anemia from which recovery was made, and in several instances the appearance of reanimation was so decided as to make the prognosis very hopeful. But after a few hours, more or less, the special senses failed, the dog became progressively stuporous, convulsions ensued, then loss

of reflexes, and, finally, respiratory failure. The decline to death indicated definitely a nervous origin, and autopsies on all the fatal cases directly following the resuscitation showed in only one organic lesion to which death could be attributed. This was a dog with anemia of eight and one-half minutes (Experiment 14) dying after between thirty and forty hours, with an early and irregularly disseminated broncho-pneumonia. As long a survival as this was the exception.

By the occlusion method, the general conclusion appears to be that ten to fifteen minutes expresses the limit within which resuscitation is practicable. This conclusion is not unassailable for two reasons: first, the impossibility of absolutely eliminating the factor of collateral circulation, and, second, the brain and cord have been separately investigated. In the latter connection, apart from the inter-relationship of the two, the possible percolation upward of the cerebro-spinal fluid,[22] with the circulation of the cord unimpeded, is worthy of consideration.

As a result of our experiments, with a certainly total anemia and little opportunity for infectious accidents—conditions the most favorable for investigation of the possibility of recovery—it is our opinion that the limit should be reduced one-half. For dogs killed by chloroform, the average duration of anemia from which recovery may be made is between six and seven minutes. The ulterior limit appears to us to be under ten minutes, and any recovery over seven and one-half minutes would be exceptional. The practical importance of the accurate fixation of the limit beyond which recovery is impossible is immense, when applied to a procedure of resuscitation which is at our disposal and may be relied upon in the case of accident.

SUMMARY.

To determine the limits of recovery after a total anemia of the central nervous system, a series of thirty dogs was killed by chloroform and resuscitated after varying times from three to fourteen minutes. Under five minutes the recovery of function was rapid and strikingly free from the after effects which characterized longer periods. Of seven animals between the periods of five and six

[22] Hill, Cerebral Circulation.

and one-half minutes, only one died apparently as a direct result of the anemia, but of twelve between the periods of seven minutes and eight and one-half minutes, only one, after seven and one-half minutes recovered. The remaining dogs all died. Further corroborative data are drawn from the previously published paper on the technique of resuscitation.

Histological examination both of presumptive recoveries and fatal cases was made by ordinary methods and those of Nissl and Marchi. The neurocytes of the fatal cases uniformly presented the greatest change, not merely chromolytic but here and there definitely indicative of cell death. Marchi's method further supported these findings by proving the existence of fiber degeneration. Finally, showing the narrowness of the escape, the animal with best result in recovery, seven and one-half minutes in time, which at the end of four weeks had apparently entirely returned to a normal state, by the Marchi method had a degeneration of a number of fibers localized in the pyramidal fasciculi which were traced from the cord to the cortex, and in Flechsig's fasciculus, as well as a more sparsely scattered degeneration of both ascending and descending fibers elsewhere.

We are indebted to Dr. H. V. Wilson, professor of zoology in the University of North Carolina, for his kindness in taking the micro-photographs.

CONCLUSIONS.

1. In dogs anesthetized by ether for preparation, and killed quickly by chloroform the average limit of total cerebral anemia, estimated from cessation of the heart sounds to return of circulation, which admits of recovery, is between six and seven minutes. The ulterior limit appears to be under ten minutes, hitherto stated as the most conservative figure, and any recovery beyond seven and one half minutes would be exceptional.

2. Further experience with resuscitation of animals killed by anesthesia and asphyxia, embracing numerous unrecorded experiments, as well as those forming the basis of the present article, establishes our former conclusion, that the procedures detailed afforded a reliable method within its limitations, and certainly uniformly successful within the limits compatible with the recovery of the central nervous system.

TABLE I.

Duration of Anemia in Minutes and Results in Recovery. (Series I.)

No. of Experiment.	Time from Beginning of Administration of Chloroform to Respiratory Failure.	Time from Respiratory to Cardiac Failure.	Duration of Recurrence of Inefficient Heart Beats After Apparently Complete Failure.*	Duration of Total Anemia.	Results.
12	4⅝	3⅙	0	3	Killed after 1 hour.
10	4¼	1½	0	4⅙	Killed after 1 hour.
17	—	3	0	4⅙	Died, 53 minutes.
3	1¼	4	0	5	Recovery.
22	2	‡	1⅓	5¼(6 1/12)	Recovery.
8	2½	½	2	5½(7½)	Killed, 24 hours.
26	†	¼	0	5¾	Killed on 4th day; secondary infection.
13	2	6	2	6(8)	Killed after 1 hour.
2	2½	1	½	6(6½)	Recovery.
23	2⅔	1¾	0	6 1/12	Died, 24 hours.
29	⅝	‡	0	6⅙	Recovery.
25	1½	4½	0	7	Died after 30–40 hours.
7	—	3¼	0	7	Died, 34 minutes.
11	7 1/12	⅙	0	7½	Died, 15–20 hours.
6	3	3	0	7½	Died, 12–20 hours.
27	2 7/12	22	0	7½	Recovery.
20	2⅓	1⅔	0	8	Died, 10–20 hours.
28	3⅓	1⅙	0	8⅙	Died, 12–20 hours.
18	—	2	0	8¼	Died, 63 minutes.
4	4	1	⅙	8⅓(8½	Died, about 12 hours.
19	2¾	1⅝	0	8 5/12	Died, about 20 hours.
14	2	1	0	8½	Died, 30–40 hours; disseminated broncho-pneumonia.
24	4½	‡	0	8½	Died, 23 hours.
1	—	6¾	0	9¼	Died, 11 hours.
9	2	2⅔	0	9⅔	Killed, 1 hour.
15	3½	½	0	9¾	Died, about 18 hours.
16	—	—	0	10	Died, 10–18 hours.
30	1 7/12	‡	0	12⅙	Died, about 2½ hours.
5	—	⅙	0	13⅓	Died, 24 hours.
21	2	‡	0	14	Died, 40 minutes.

*As noted on page 786 this column refers to the spontaneous recurrence of the heart sounds in five cases from one-third to one and a half minutes after they had entirely ceased. As the extent of the circulatory recovery could not be exactly estimated, though usually it was not sufficient to produce a palpable pulse, in the next column the duration of the total period without any evidence of cardiac activity is given first, while the figures in parenthesis include the partial recovery.

† Asphyxiated dog.

‡ Synchronous.

TABLE II.

Results in Recovery of Series I.

(In other successful experiments the animals were killed after shorter interval.)[28]

Number of Experiment.	Total Duration of Anemia.*,	Mode of Death.	Results.
28	7½	Ether.	Killed, 24 hours; resumptive recovery.
19	8½	Asphyxia.	Killed, 6 hours.
31	9½	Chloroform.	Died, 20 hours.
37	9½	Chloroform.	Died, 20 hours.
48	12	Asphyxia.	Died, 3¾ hours.
39	13½	Chloroform.	Died, 15 hours.
41	15	Chloroform.	Died, 15 hours.
30	16⅓	Ether.	Died, 3½ hours.
43	24	Chloroform.	Died, 4½ hours.
49	32	Chloroform.	Died, 27 minutes.

* Includes time spent in resuscitation.

TABLE III.

The Course of Blood-pressure after Resuscitation. (Series I.)

(The time is in minutes after restoration of circulation and the pressure in mm. Hg.)

Number of Experiment	Duration of Anemia.*	Time of Respiratory Recovery.	Maximum B. P. after Resuscitation.	Time to Reach First Lowest Level.	Lowest Level of B. P.	Approximate Duration of Lowest Level.	Total Time to Second Rise.	Height of Second Maximum.	Subsequent Course (x)
28	7½	4½	240	10½	80	†	11	160	Maintained for 24 hours.
19	8½	11½	206	14½	130	‡			Maintained for 6 hours.
31	9½	7	210	30	80	‡			Removed from table.
37	9½	½	230	40	80	‡	40	90	Removed from table.
48	12	16	220	16	50	10	36	80	Fell after 5 minutes.
39	13½	15½	250	18	80	2	20	120	Fell shortly to 70 mm.; 1 hour.
41	15	8¾	180	28	44	15	43	88	Removed from table.
30	16⅓	15½	144	23	118	3	26	140	Fell after 10 minutes.
43	24	4	110	23	36	5	28	70	Second maximum held 1 hour.
49	32	21	114						Cardiac failure after 27 minutes

* Includes approximate time of the act of resuscitation.

† Immediate rising tendency.

‡ Level steadily maintained.

§ Removed from table in 30 minutes.

|| In general, a decline to death.

[28] Crile and Dolley, *Jour. of Exper. Med.*, 1906, viii, 713.

TABLE IV.

Giving Time in Minutes of Recurrence of Respiration and Various Reflexes after Restoration of Circulation. (Series I.)

No. of Experiment.	Duration of Anemia.	Respiration.	Corneal Reflex.	Winking.	Light Reflex.	Knee-jerk.	Cutaneous Reflex (First).
12	3	2	4¾	5	38	16	—
10	4⅙	1⅔	10	10½	18½	10	13½
17	4⅙	2⅔	20	25	0	0	0
3	5	⅔	2	*	10¼	2	—
22	5¼	1¾	*	15¾	128	17	23
8	5½	2	13½	16½	18½	12	—
26	5¾	—	12½	—	14½	24½	—
13	6	7 1/12	*	19	†	35	39
2	6	¾	10¾	13	40	8¾	25
23	6 1/12	2	10½	19½	‡	31½	32½
29	6⅙	⅓	5⅙	7½	94	11⅙	17⅔
7	7	1	0	0	0	0	0
25	7	2 7/12	*	Under 15	29	Under 15	Under 15
11	7½	4¾	17	23	34	17	34
6	7½	14	29½	36	33½	28½	—
27	7½	2	12½	20¾	53½	14½	24½
20	8	3	21	*	0	21	66
28	8⅙	1 1/12	17 5/6	34	68	*	42
18	8¼	2⅔	20	25	0	0	0
4	8⅓	2½	*	18½	0	23½	33½
19	8 5/12	1	15	35	62	17	60
14	8½	1¼	*	18½	0	17	—
24	8½	1 1/12	14 7/12	38	‡	*	53
1	9¼	4¼	61½	*	98½	74½	—
9	9⅔	8	25	35	†	20⅔	—
15	9¾	1½	16	34	0	14	49
16	10	6	28	38	‡	28	—
30	12⅙	2¼	12 1/12	23¾	32	25¾	28¾
5	13⅓	4	16	16	60+	14	16
21	14	3	0	0	0	0	0

* Recurred; exact time not noted.

† Insufficient time.

‡ Did not return under observation.

EXPLANATION OF PLATES.

PLATE XLIX.

FIG. 1. Microphotograph of a left dorso-lateral segment of the spinal cord from the cervical region. Stained by the Marchi method. The degeneration is almost entirely localized to the fasciculus lateralis pyramidalis and the fasciculus lateralis proprius (Flechsigi). The splotch in the gray matter is a negative defect. From Experiment 27; puppy eight months old; death by chloroform; resuscitation after 7 minutes and 30 seconds; return to an apparently normal condition in about three weeks; and examination after another week. (Zeiss Planar 2, B. & L. oc. 2.)

FIG. 2. Microphotograph of the fasciculus lateralis pyramidalis from the same section as I with higher magnification. (Experiment 27; Marchi method; Zeiss obj. A. B. & L. oc. 2.)

PLATE L.

FIG. 3. Microphotograph showing adjoining portions of the pyramids of the medulla, also from the same case as Figs. 1 and 2. Outside of these, there is only an occasional degenerated fiber, and higher sections traced the degeneration to the motor cortex. (Zeiss obj. A. B. & L. oc. 2.)

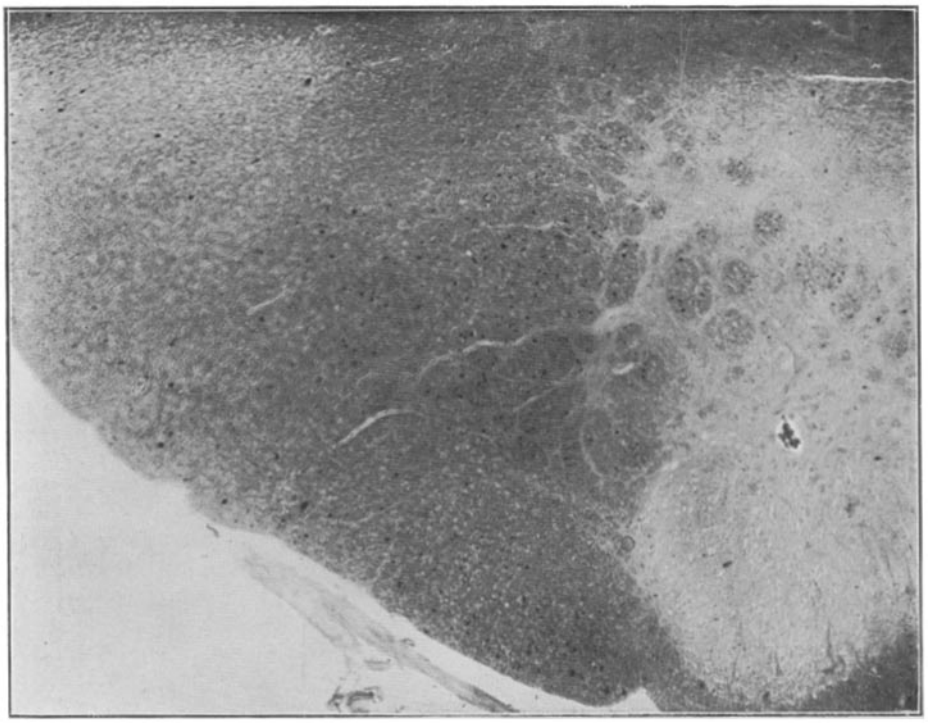

FIG. 1.

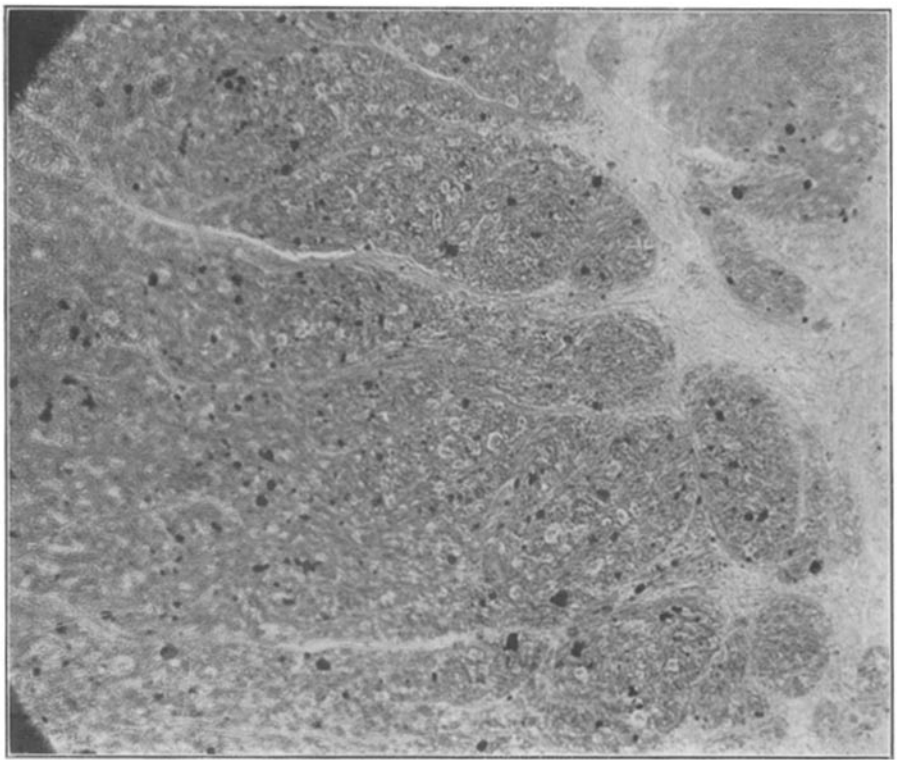

FIG. 2.

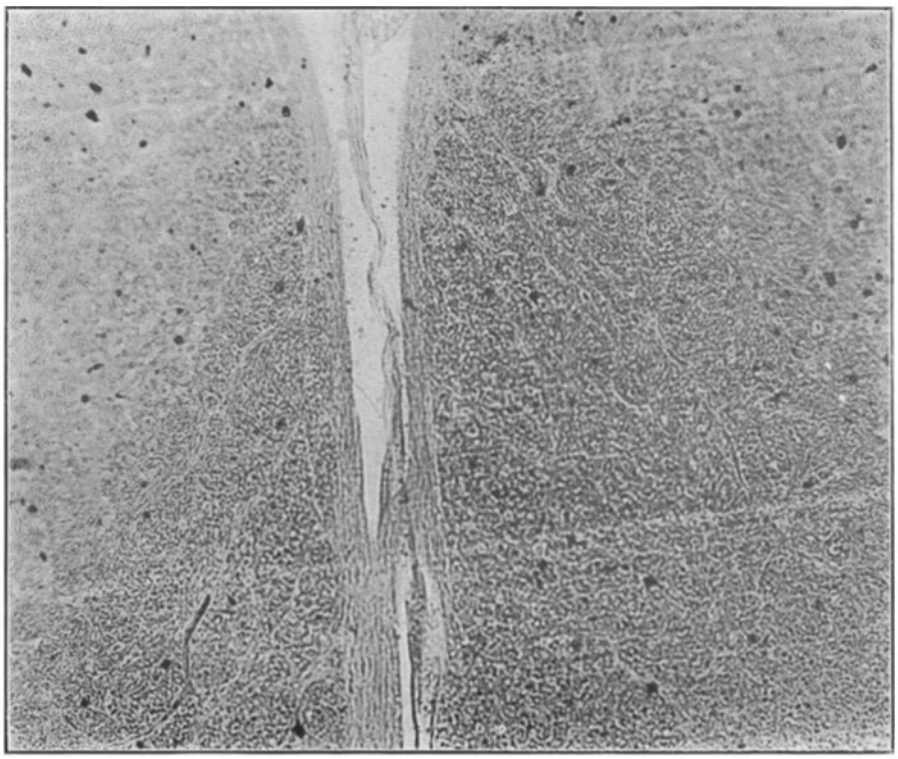

FIG. 3.