ON THE RESTORATION OF THE NEUROREFLEX REGULATION OF THE CARDIOVASCULAR SYSTEM DURING RESUSCITATION AFTER CLINICAL DEATH

D. G. Maksimov

Laboratory of Experimental Physiology of Resuscitation
(Head, Prof. V. A. Negovskii) Academy of Medical Sciences, USSR, Moscow
(Presented by Active Member, AMS USSR, V. V. Parin)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 52, No. 10,
pp. 34-38, October, 1961
Original article submitted December 22, 1960.

The stability of the restoration of the cardiovascular system during resuscitation is closely connected with the restoration of the central nervous system and the resumption of the neuroreflex regulation [10, 12, 13]. In the beginning of the resuscitation after clinical death only elementary reflex reactions can be observed in the caridovascular system [12, 18, 19]. A higher level of neuroreflex regulation can be observed after the function of the respiratory center has been restored [10, 11, 12].

It was the aim of the present paper to study the restoration of the neuroreflex regulation in the cardiovascular system during resuscitation after clinical death, caused in various ways. We paid particular attention to changes in the regulation of the cardiovascular system, connected with the restoration of the respiratory function.

EXPERIMENTAL METHOD

The experiments were carried out on adult dogs, weighing 10-15 kg. Before the actual experiment we prepared the femoral blood vessels, under pantopon-ether narcosis or under local anesthesia, with 0.5% novocain solution. In 35 dogs the clinical death was brought about by bleeding, in 18 dogs by mechanical asphyxia and in 15 dogs by electric trauma (induction of cardiac fibrillation by connecting the heart with the alternating current mains at a tension of 127 V). Death occurred in the dogs which were bled out within $3\frac{1}{2}$ - 38 min, and in cases of mechanical asphyxia or electric trauma within 3-10 min. In various experiments the state of clinical death lasted between 1 and 15 min. The dogs were resuscitated by the method developed by V. A. Negovskii and co-workers[7, 10, 12]. During the experiments we recorded the arterial blood pressure, the electrocardiogram and the respiratory movements of the chest. The early stages in the stimulation of the respiratory center, which became manifest in movements of the tongue and neck muscles were marked on the kymogram with crosses.

EXPERIMENTAL RESULTS

The appearance of the first respiratory movements during the resuscitation was accompanied by reactions of the cardiovascular system, reactions which varied depending on the speed at which the death had occurred and on the duration of the state of clinical death. In this context the cause of death was of secondary importance. If the death had occurred slowly (more than 15 min) or if the state of clinical death had lasted for a long period (over 6 min) the excitation of the respiratory center became initially manifest only in movements of the tongue and neck muscles. The response of the cardiovascular system to these movements became manifest in a shortlasting rise in the arterial blood pressure without changes in the cardiac rhythm or in the shape of the electrocardiogram.

As soon as the respiratory movements of the chest had been resumed, the character of the cardiovascular response to the act of inspiration changed: instead of an increase a temporary fall could be observed in the arterial blood pressure (Fig. 1 b). In the electrocardiogram a slowing down of the pulse rate instead of the usual inspiratory tachycardia could be observed, the atrial P wave was flattened and the atrio-ventricular conduction time was prolonged (Fig. 2 c). Parallel to the increase in the depth of the respiratory movements the above signs became more marked. Simultaneously the mean arterial blood pressure rose and the heart rate became less frequent.

3-7 min after the resumption of the respiration the mean arterial blood pressure decreased and the respiratory variations in the blood pressure became less intensive (Fig. 1 c, d). The inspiratory bradycardia became gradually

less marked and was later replaced by the usual inspiratory tachycardia (Fig. 2 d). Simultaneously with the restoration of the normal type of respiratory arrhythmia the electrocardiographic changes connected with the respiration reverted to their normal character (greater amplitude of P-wave and shortening of the P-Q interval during inspiration). The normal response of the cardiovascular system to the act of inspiration was restored within 15-30 min after the beginning of the resuscitation.

If the hypoxia had been less marked (death occurring within 10 min and clinical death lasting not longer than 6 min) the initial excitation of the respiratory center became immediately manifest in chest movements. In this case the response to inspiration began directly with a fall in the arterial blood pressure and a slowing down of the heart rate. The subsequent changes were similar to those described above. The usual cardiovascular response to inspiration was restored 7 - 15 min after the beginning of the resuscitation.

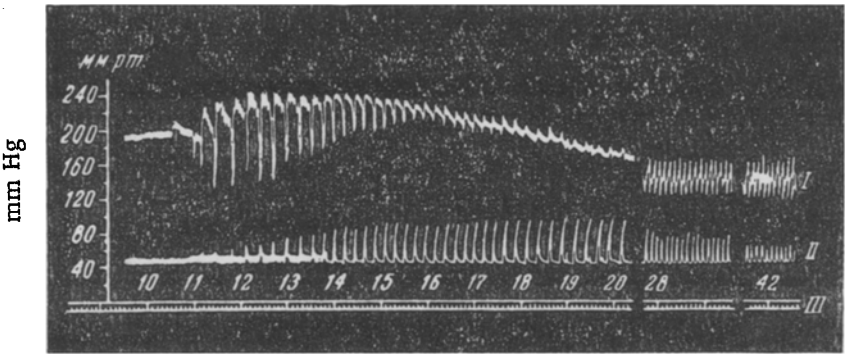

Fig. 1. Changes in the arterial blood pressure in connection with the resumption of respiration during resuscitation of a dog from a state of clinical death, lasting 5 min. (The death caused by bleeding had occured within 23 min). I) Recording of the arterial blood pressure; II) recording of the respiratory chest movements; the crosses indicate the initial weak respiratory movements; III) the zero line (under this line the time is marked; the numbers above the zero line indicate the time elapsed since the beginning of the resuscitation in min; a) before the resumption of the breathing; (the slight variations in the arterial blood pressure are caused by artificial respiration); b) the marked fall in arterial blood pressure during the inspiration at the time when the respiratory chest movements begin to reappear; c) less marked fall in the arterial blood pressure at the time of inspiration and deeper breathing; d) shortlasting rise in the arterial blood pressure during inspiration; e) restoration of the normal type of respiratory variations in the arterial blood pressure with an initial fall in the pressure at the beginning of the inspiration and a subsequent rise; f) preservation of the usual type of respiratory variations in the arterial blood pressure (with an increased amplitude). During the restoration of the respiration the mean arterial blood pressure first increases and later decreases again. The response of the arterial blood pressure to the inspiration undergoes phasic changes.

As soon as the reflexes to pain and the tendon reflexes were restored – particularly after prolonged hypoxia – external stimuli elicited, in addition to the adequate response, an unusually strong cardiovascular response, consisting in a marked increase of the arterial blood pressure and of the heart rate. After the reappearance of the pupillary reflex, i.e. with the beginning restoration of the mesencephalic function, the pathological character of the cardiovascular response to external stimuli became less marked. The inadequate character of the response, however, persisted for several days after the experiment.

Full restoration of the nervous regulation of the cardiovascular system occurred, after a short dying process and a shortlasting state of clinical death, within 1-2 weeks; if death occurred more slowly, or if the state of clinical death was prolonged, within 4 weeks or later. Other authors observed similar periods [9, 21].

Normally the respiratory arrhythmia in dogs can be explained, as is well known, by a decrease in the tonus of the n. vagus during inspiration. In young puppies, in which the regulation of the cardiac rhythm by the n. vagus is undeveloped [1, 2, 20], no respiratory arrhythmia can be observed [6]. Later after the development of the vagus regulation and the fall in the heart rate [2, 4] respiratory arrhythmia begins to appear [6]. Transsection of the n. vagus or injection of atropin leads to an increase in the pulse rate and a disappearance of the respiratory arrhythmia in adult dogs [3, 15, 22].

Above, we were able to show that the respiratory arrhythmia observed during the restoration of the breathing after clinical death is of a distorted character. Instead of the usual increase in the heart rate during the inspiration the reverse phenomenon, a decrease in the heart rate, can be observed. In view of the high pulse frequency during

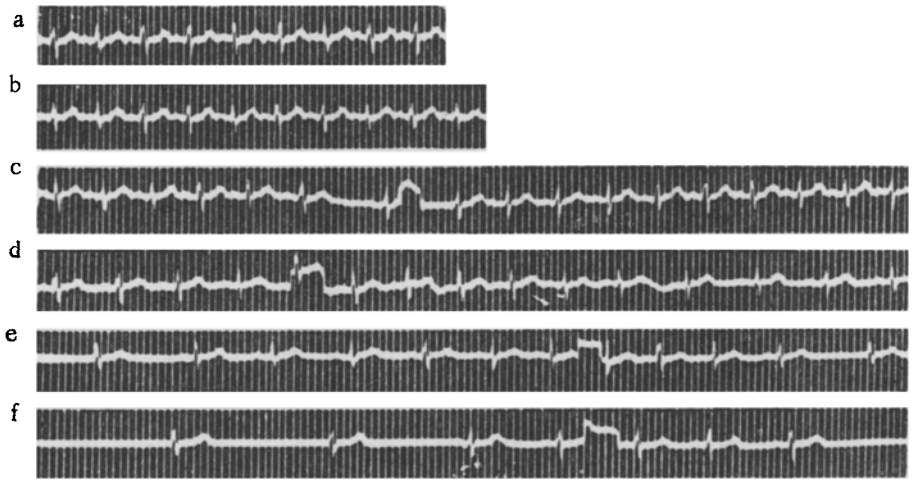

Fig. 2. Electrocardiographic changes in relation to the restoration of the breathing in the experiment, the results of which are shown in Fig. 1. (The beginning of the inspiration is marked by the millivolt signal). a) Before the restoration of the breathing (the pulse frequency reaches 193 beats per min); b) after the second respiratory movement of the chest (no significant changes in the electrocardiogram); c) $2\frac{1}{2}$ min after the restoration of the breathing (distorted response to the inspiration: slowing down of the pulse rate and prolonged atriventricular conduction time); d) $7\frac{1}{2}$ min after the restoration of the breathing (slowing down of the heart rate to 150 beats per min and appearance of the usual respiratory arrhythmia: increased pulse rate during the inspiration); e) – f) $17\frac{1}{2}$ and 31 min after the restoration of the breathing (marked respiratory arrhythmia and further slowing down of the pulse rate).

that period (Fig. 2b) it can be assumed that during the resuscitation the vagus center begins to function periodically – only during the inspiration. This can be explained with the assumption that the restoration of this function is closely connected with the rhythmical stimulation by the respiratory center. Later, after the permanent tonus of the vagus center has been restored, the reverse situation develops: during the stimulation of the respiratory center the heart rate increases during the inspiration instead of the previous decrease.

It is interesting that after the reappearance of the breathing the increase in the arterial blood pressure initially also occurs only during the inspiration. Hence the function of the vasomotor center also depends at the beginning stage of resuscitation on the periodic stimulation by the respiratory center.

After the function of the n. vagus has been restored the response to inspiration takes on a more complex character: the stimulation of the vasomotor center is masked by the simultaneous stimulation of the vagus center and the decrease in the heart rate; in consequence the arterial blood pressure decreases during the inspiration. After the respiratory arrhythmia has reverted to its normal type no fall in the arterial blood pressure can be observed at the beginning of the inspiration (see Fig. 1d; 2d). Somewhat later the respiratory variations in the arterial blood pressure revert to the normal character; at the beginning of the inspiration there is a slight fall in the blood pressure, due to the decreased vascular tonus at this stage of respiration [16, 17, 23]. The restoration of the regulating influence, exerted by the vasomotor center upon the cardiovascular system, thus undergoes the same evolution as the restoration of the vagus center. In both cases the normal nervous regulation is restored after a paradoxical phase.

The inadequate character of the response to external stimuli by the cardiovascular system, during the first hours and days of resuscitation, might be explained with disorders in the inhibitory process within the central nervous system. V. A. Negovskii suggested that the state of excitation possibly irradiates over a wide area of the central nervous system at the beginning of the resuscitation [10, 13]. Irradiation of this type from the respiratory center into the cerebral cortex could be established electroencephalographically in the shape of periodic oscillations appearing on the electroencephalogram in step with the respiratory rhythm [5]. A weakening in the inhibitory function could be demonstrated in a number of studies on the conditioned reflex activity of the cerebral cortex, during resuscitation after clinical death [8, 13, 14].

The data in the literature and the results of our own investigations thus warrant the assumption that, during the initial stages of resuscitation, the cardiovascular system is mainly under the influence of the sympathetic nervous system. The restoration of the regulation by the vagus center begins after the breathing function has been resumed. Full restoration of the neuroreflex regulation of the cardiovascular system takes place after the recovery of the higher parts of the central nervous system.

SUMMARY

Investigations carried out by the author have demonstrated that in reviving the organism after clinical death the activity of the vagus center is restored subsequent to the appearance of respiration. Up to that time the cardiovascular system was under a preponderant effect of the sympathetic nervous system. In the next few days following the revival, the heart reactions to external stimuli were inadequate. This may be due to an incomplete central nervous system restoration. Cardiac reaction to external stimuli normalized in 1 - 4 weeks.

LITERATURE CITED

1. I. A. Arshavskii, The Nervous Regulation of the Cardiovascular Function during Ontogenesis [in Russian] (Moscow-Leningrad, 1936).
2. I. A. Arshvaskii, The Physiology and Pathology of the Cardiovascular System [in Russian] (Leningrad, 1941)p. 73.
3. I. A. Arshavskii, Problems of Soviet Physiology, Biochemistry and Pharmacology, Part I [in Russian] (Moscow, 1949) p. 410
4. I. A. Arshavskii, The Nervous Regulation of Circulation and Respiration [in Russian] (Moscow, 1952) p. 62.
5. A. M. Gurvich, Fiziol. Zhurn. SSSR, No. 4 (1960) p. 434.
6. S. I. Enikeeva, Fiziol. Zhurn. SSSR, No. 2 (1955) p. 227.
7. Instruction concerning the Methods to be Employed for the Restoration of Vital Functions in Patients in Terminal States [in Russian] (Moscow, 1959).
8. A. R. Kotovskaya, Changes in the Higher Nervous Activity of Dogs After Resuscitation, Dissertation [in Russian] (Moscow, 1958).
9. A. I. Makarychev, A. V. Popova, and T. N. Grozdova, Summaries of Reports of the Scientific Conference on Problems of Experimental Pathophysiology and Therapy of the Higher Nervous Activity in Animals [in Russian] (Moscow, 1957) p. 70
10 V. A. Negovskii, Restoration of the Vital Functions in Agonal States or During Periods of Clinical Death [in Russian] (Moscow, 1943).
11. V. A. Negovskii, Byull. Éksper. Biol. i Med., 15, No. 6 (1943) p. 37.
12. V. A. Negovskii, The Pathological Physiology and Therapy of Agony and Clinical Death [in Russian] (Moscow, 1954).
13. V. A. Negovskii, Resuscitation and Artificial Hypothermia [in Russian] (Moscow, 1960).
14. V. A. Negovskii, A. I. Makarychev, and A. V. Popova, Zhurn. Vyssh. Nervn. Deyat., No. 4 (1956) p. 584.
15. P. M. Nikiforovskii, Izv. Voen.-Med. Akad., 21, No. 3 (1910) p. 221.
16. V. V. Parin, Byull. Éksper. Biol. i Med., 15, No. 3 (1943) p. 28.
17. N. Rozhanskii, Trudy Fiziologicheskoi Laboratorii Donsk. Un-ta, No. 2 (Rostov-on-Don, 1920) p. 3.
18. E. M. Smirenskaya, Transactions of the Conference on the Problem of Pathological Physiology and Therapy of Terminal States in Clinical and Casualty Practice [in Russian] (Moscow, 1954) p. 38.
19. E. M. Smirenskaya, Problems Concerning the Compensation and Experimental Therapy of Radiation Sickness, (Moscow, 1960) p. 78.
20. E. I. Turbina-Shpuga, Med-Biol. Zhurn., No. 4 (1929) p. 39.
21. H. Bergmann, K. Müller, and W. Pilgerstorfer, Wien. Med. Wschr., No. 105 (1955) p. 761.
22. E. Blumenfeld, and H. Putzig,Pflüg. Arch. Ges. PhysioL, No. 155 (1914) p. 443.
23. E. Gerstenberg, U. Wagenmann, E. Schmid, and R. Taugner, Arch. Exp. Path. Pharmak., No. 229(1956) p. 520.