PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

RESTORATION OF VITAL FUNCTION IN MONKEYS AFTER BLEEDING TO DEATH DURING HYPOTHERMIA

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It has been shown recently both in clinical and laboratory work that the central nervous system is considerably more resistant to temporary interruption of the circulation when the temperature is artificially reduced. Previous laboratory investigations have shown that artificial cooling enables the period of "clinical death" in dogs caused by exsanguination to be increased from the normal value of 5-6 minutes up to one hour, and that afterwards there may be a complete recovery [2].

We have carried out similar experiments on monkeys as representing animals at higher stages in evolution, so that the results might be more closely applicable to clinical practice. There are not many reports dealing with hypothermia in monkeys, but it has been emphasized [4, 7, 8, 9] that in such experiments certain specific features of monkeys distinguish them from other animal species.

METHOD

The experiments were carried out on 10 monkeys of both sexes, chiefly hamadryads, age from 3 to 14 years, and weighing from 6 to 26 kg.

Injections of 1.5 ml per kg of a 2% solution of pantopon, and 0.1 mg per kg of a 0.1% atropine solution were given before the experiment. The temperature was reduced by surrounding the animal with ice packs.

Before and during the cooling, an intravenous drip of 0.2% pentothal solution was given. Clinical death during the hypothermia was caused by bleeding from the femoral artery.

Restoration of vital function was brought about by a complex method which consisted of forcing the arterial blood in towards the center, applying artificial respiration, and in many cases by massaging the heart directly. When the heart began to fibrillate, a single electrical impulse was applied to it. Immediately the heart began to beat; in order to combat the acidosis, an intravenous injection of 0.15 g per kg of sodium bicarbonate in an 8% solution was given. In most of the experiments the body temperature was raised by immersing the animal in water at 43-45°.

RESULTS

As has already been pointed out, the animal was cooled during pentothal anesthesia. The total amount of pentothal injected varied from 70 to 150 ml. In spite of the fact that two to three times less pentothal was given to monkeys than to dogs in similar experiments, it was found that the monkeys were exceptionally sensitive to

this anesthetic. In 5 of the 10 animals, the respiration became irregular during the cooling, particularly during the first hour, Cheyne-Stokes breathing occurred, and sometimes even this kind of breathing ceased. It was therefore neccessary to apply artificial respiration during cooling. On the other hand, if the pentothal injection was discontinued for a short period, the animal recovered from the anesthetic and an active reaction to the cold took place. An increase of approximately 10 times in the toxicity of anesthetics in the cold has been repeated [5]. In the remaining 5 monkeys, nothing but a slight slowing of the respiration rate was observed.

In 2 of the 10 monkeys, after 1 hour, 48 minutes and after 2 hours, 2 minutes from the beginning of the cooling, when the body temperature had fallen to 27.3°, extra-systoles appeared, and these indicated the onset of fibrillation. In 1 monkey the fibrillation was rapidly eliminated, while in the other, repeated attempts to do so were successful only for a short time, after which it again reappeared. Fibrillation continued for 25 minutes. During this time respiration ceased. Subsequently, elimination of the fibrillation, warming the animal, intravenous injection of warm polyglucin solution, and artificial respiration restored the heartbeat and respiration. After 2 hours from the onset of cooling, the monkey was once more in good condition. Thus, unlike other animals, the monkeys tolerated clinical death occurring as a result of cardiac fibrillation even when this developed during the cooling process.

In the remaining 9 animals, 1 hour, 13 minutes and 2 hours, 30 minutes from the onset of cooling when the temperature had fallen to 26.2-28.5°, bleeding was continued. The arterial pressure fell from 120-150 to 72-100 mm mercury. The highest pulse rate before the experiment was 150-200 per minute, and during bleeding it fell to 58-100 per minute. The duration of the ventricular complex increased from 0.2 to 0.35 second. Changes in the electrocardiogram consisted of a marked increase in the amplitude of the negative going wave, in an expansion and division into two of the R notch and the appearance of an extra spike on the initial portion of the S-T wave ("injury potential"). It must be noted that this change was observed in dogs only when the temperature was cooled below 25°. The respiration rate varied from 11 to 22 per minute.

In 8 of the 9 animals, the time taken to die varied from 42 minutes to 2 hours, 16 minutes, i.e., it was considerably longer then in the corresponding experiments on dogs. Only in one monkey was the period shorter, lasting 22 minutes, 10 seconds. In one animal respiration ceased during cooling but before bleeding, and for the first 11 minutes of the period for which the animal was dying, artificial respiration was maintained before natural breathing was restored.

The long time which the animals took to die in some of the experiments must be explained as being due to very highly developed compensation. Thus, for instance, during the bleeding, and particularly when it was first begun, there was frequently a spasm of the peripheral vessels. The amount of blood which was obtained by free bleeding was not more than 30-50% of the total amount. In 6 out of the 9 animals, after regular respiration had ceased, a period of agony ensued, and lasted for 11-20 minutes. Despite the fact that long before the agony, at the 8-15th minute of the dying period, the arterial pressure fell to zero, respiration was maintained for as long as from 25 to 42 minutes, and in one experiment continued for as long as 2 hours after the fall in arterial pressure. The long-maintained functioning of the respiratory center in monkeys at blood pressure levels approximating to zero must be regarded as a special form of compensation which is far more highly perfected than in dogs, where such an event never occurred. The early spasm of the peripheral vessels, by reducing blood loss, maintains an adequate oxygen supply for a considerable period [3] and so protects the nervous centers. Support for this view is supplied by clinical observations in which consciousness is maintained in dying individuals in whom no blood pressure can be recorded.

Before bleeding there was little change in the ECG. As the hypoxia increased, the P wave became broader and there was a displacement of the S-T interval upwards, so that the ventricular complex showed up as a monophasic deviation. During the terminal pause and cessation of sinus control, occasional biphasic complexes occurred in abnormal positions.

Clinical death lasted from 10 to 30 minutes. At the end of this period the body temperature was 21-27.2°. In one monkey it was below 17°. During this time occasional monophasic excursions of the line corresponding to the ventricular complex were observed on the ECG. Usually these disappeared completely by the 5-10th minute, and if no fibrillar oscillations occurred, there was no further ECG activity until the blood was forced into the arteries.

The heartbeat was restored in from 27 seconds to 2 minutes from the beginning of resuscitation. As the blood was driven into the arteries, ventricular complexes began to appear on the ECG, and the changes observed

were the reverse of those recorded while the animal was dying. The return of the ECG to its original level occurred when the body temperature was raised to 32-34°.

With the exception of two animals, after the heartbeat had been restored, there was fibrillation. In many of the monkeys it was rapidly eliminated by applying a single electrical impulse to the heart. In 4 animals it returned many times during the first 22-34 minutes of recovery. Spontaneous arrest of the fibrillation occurred frequently, both while the animal was dying, during clinical death, and during recovery, though this never happened in dogs. Subsequently, however, fibrillation again returned, when it was once more eliminated electrically. Subsequent arterial injection of warm blood with added glucose and hydrogen peroxide led to permanent restoration of normal heart function. Cases have previously been reported of spontaneous cessation of fibrillation in monkeys [6].

In one experiment, an ineffectual heartbeat was restored by massaging the heart and driving the blood into the arteries 1 hour, 29 minutes after the onset of recovery. During the whole of this time the heart fibrillated, evidently due to the low temperature of 17°.

After the restoration of heart function, the weak beat had to be maintained by massage. Respiration was restored 2 hours, 15 minutes from the beginning of cooling, and then again failed.

In the remaining animals the respiration was restored at times from 3 minutes, 15 seconds to 24 minutes after the beginning of recovery, when the body temperature was 23-27°. In 4 monkeys it was restored, but the heart fibrillated. Short-term restoration of the beat in the fibrillating heart which sent a periodic supply of blood to the brain, and artificial respiration restored normal breathing before the normal heartbeat returned. In one experiment the respiration was never re-established. The respiration returned to normal rapidly (after 60-90 minutes), and such an effect is now found in dogs. It may be to some extent associated with the action of the bicarbonate. Several descriptions have been given [1] of the rapid restoration of breathing after injecting bicarbonate into animals who have survived 5 or 7 minute periods of clinical death at normal temperatures.

In monkeys, the pupil reflexes were restored 24 to 57 minutes after the beginning of recovery when the body temperature had values between 24.1 and 30°.

In 5 of the 9 animals, the recovery of the heartbeat and the respiration was only temporary. After recovering, the animals died from pulmonary edema, 2 dying on the operating table and one at the end of the first day. Drawing off the fluid, bleeding, injecting of calcium chloride and 40% glucose, did not prevent the development of edema. In another animal, death occurred during heart massage when the artificial respiration was wrongly applied and pulmonary tissue was torn, the need for a right pneumothorax being realized too late. It must, however, be appreciated that two of the monkeys which died were of the Macaque-Lapunder breed. These animals are extraordinarily sensitive to operative measures, they do not become acclimatized or breed in the conditions obtaining in Sukhumi.

Complete restoration of vital function in animals which have survived clinical death from bleeding during hypothermia occurred in 4 of the 9 monkeys. Two of these survived a 10 minute period of clinical death, 1 a 20 minute period, and in 1 the condition lasted for 30 minutes. It is important to note how rapidly vital function was restored in these cases. Hearing and sight returned after 4-10 hours from the beginning of cooling. After 10-18 hours, they were able to stand unaided. For a short time there was some discoordination of movements. Complete and permanent recovery occurred after 19-48 hours. Recovery was particularly rapid in the animal which had been in a condition of clinical death for 30 minutes. After 6 hours, 30 minutes from the beginning of recovery, its outward appearance was almost normal.

Thus, by means of hypothermia it was possible to extend clinical death from bleeding for as long as 20-30 minutes.

It must be noted, however, that unlike dogs, even under hypothermic conditions, monkeys were more sensitive to severe hypoxia caused by bleeding to death. Recovery in these cases represents a more complex process. Thus, for instance, of the 4 monkeys which survived 30 minute periods of clinical death, only one recovered completely.

At the same time it is known that hypothermic dogs which have survived such periods as a rule recover permanently [2].

Also, when monkeys recover, vital function returns considerably more rapidly than in dogs, and this is evidently to be ascribed to their more highly perfected compensatory processes.

SUMMARY

Clinical death resulting from acute blood loss in monkeys was prolonged up to 20-30 minutes with the aid of hypothermia. Vital function was restored by means of centripetal arterial blood transfusion and artificial respiration; direct cardiac massage and elimination of defibrillation by electrical stimulation were used in a number of cases. Monkeys are, however, more sensitive to the hypoxia caused by bleeding to death than are dogs, even under hypothermic conditions. Thus, complete restoration of vital function was achieved only in 1 monkey out of the 4 which sustained a 30 minute period of clinical death. At the same time, when the monkeys recover, vital function is restored more rapidly than in dogs. The latter is evidently due to more perfect compensation.

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