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THE EFFECTS OF ACUTE HAEMORRHAGE ON THE PERIPHERAL BLOOD PRESSURE IN UNANAESTHETIZED AND IN ANAESTHETIZED RABBITS

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The consequences of haemorrhage in animals have been frequently described, but few observations have been made on the effects of a single acute loss. It is also of interest to note that investigators have paid little attention to the complicating effects of anaesthesia.

The experiments described below were undertaken to study the effects of a single acute haemorrhage on the arterial pressure and heart rate of unanaesthetized and anaesthetized rabbits.

Method

Adult rabbits fed on a mixed diet were used. Body weight varied between 1·4 and 3·7 kg. In early experiments the systolic pressure in the central artery of one ear was estimated by the method of Grant & Rothschild [1934]. Heart rate was counted by two observers simultaneously, using two sets of ear-pieces attached to the stethoscope bell. Later, an optical method of recording systolic pressure and pulsations of the ear artery was developed [Downman, Mackenzie & McSwiney, 1944]. The experiments were done in a warm room, and care was taken to ensure that the ear vessels were fully dilated before making observations. As the ears became warmer, the arteries dilated, but would contract if the ear was handled; later this irritability was lost, and the vessels did not respond to handling the ear [Downman *et al.* 1944]. Uniform series of pressure readings could now be obtained and there was no contraction of the arteries when the other ear was cut. Repeated observations of systolic pressure and heart rate were made to ascertain that a steady state was reached before bleeding. Unanaesthetized animals were restrained in a wooden box, with the head protruding through a hole in one side, and were not disturbed during the experiment.

In the normal blood-pressure range the systolic pressure in the dilated ear artery lies only 2–5 mm. Hg below the mean carotid pressure. At low pressures, such as occur after bleeding, differences of 20–30 mm. Hg have been observed. The pressures recorded in these experiments must, for the present, be recognized only as samples of peripheral arterial pressures.

Blood was taken from the large vein at the base of the other ear. The dorsal surface of the ear was shaved and the skin around the site of the proposed incision smeared with vaseline to prevent blood spreading. A quick cut with a sharp scalpel along the long axis of the vein divided the skin and the wall of the vessel. The blood was collected in small beakers.

To produce general anaesthesia urethane dissolved in normal saline was injected into the marginal vein of the ear. One group of animals received 1·4–1·6 g. urethane per kg. body weight; another group received 1·64–1·9 g. per kg. The effects of the different doses are described later.

Results

Unanaesthetized rabbits

On cutting the vein, blood flowed rapidly for from 3 to 5 min. The flow then slowed quite suddenly; oozing continued for several minutes and then ceased entirely.

The volume of blood lost varied from 12 to 51 ml., but with one exception this did not exceed one-third of the calculated blood volume. Assuming that adult rabbits have a blood volume of 70 ml./kg. body weight [Courtice, 1943], these losses represented 7–33% of the blood volume or 0·5–2·3% of the body weight. The one exceptional animal lost 36% of its blood volume.

The animals were not obviously distressed by the haemorrhage even though nearly one-third of the blood volume was lost in 4–5 min. There was, however, an increase in the rate and depth of breathing. All unanaesthetized animals bled in this manner survived.

The ears remained warm and the main vessels showed no change of diameter to the naked eye during and after bleeding. Small areas of the ear were sketched at intervals before and after venesection; there was no apparent alteration in the size or number of the visible vessels, nor did the arterial pulse volume decrease perceptibly. There was in some animals, nevertheless, evidence of contraction of the minute vessels, shown by slight pallor of the ear tissues. This continued for some hours after bleeding.

Cessation of bleeding occurred after the initial fall of blood pressure. The pressure was recovering quickly at the time and may even have reached the initial level. Furthermore, the pressures recorded from the cut ear were the same as those in the other ear. The end-point was not influenced by intravenous heparin, nor by anaesthetizing the tissues round the incision with 2% procaine solution. These results suggest that the cessation of bleeding is not dependent primarily upon blood-pressure fall, altered blood coagulability, nor extrinsic nervous mechanisms. During and after the bleeding the vein remained dilated, except at the cut and for 2–3 mm. beyond each end of the cut. If saline was injected into the vein towards the cut, through a needle inserted distal to the cut, a pressure of 10–20 mm. Hg was needed to cause saline to flow through the constricted portion of the vein. When the vein was then occluded proximal to the cut a perfusion pressure of 100 mm. Hg was needed to open the cut. When bleeding ceased, manipulating and rubbing the cut caused no further loss of blood, but an hour later the same treatment resulted in copious bleeding. It seems that in these animals the haemostasis was produced by a powerful localized spasm of the vein wall set up and maintained by local means. The spasm passes off within the hour but meanwhile the cut edges of the vein have become stuck together. The walls can be unstuck again by manipulation.

Blood-pressure change. One to three minutes after the onset of bleeding systolic pressure in the ear artery fell steeply from the initial level of about 100 mm. Hg down to 30–40 mm. Hg. Almost at once the pressure started to rise quickly even though bleeding continued. The subsequent changes of blood pressure were of three types. In the first type, the recovery of pressure continued and pre-haemorrhage readings were obtained in 10–20 min. In the second type, the recovery of pressure approximated to only two-thirds of the initial fall in 40 min.; subsequently pressure fell again to 40 mm. Hg, and there was a slow return to the initial level. In the third type, the recovery amounted

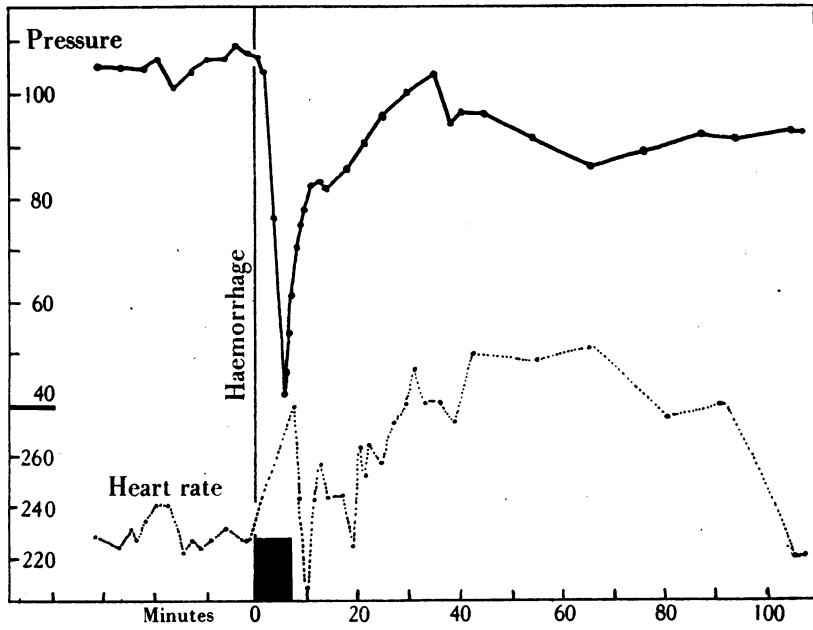

Fig. 1. Changes of systolic pressure in ear artery and of heart rate, in unanaesthetized rabbit. The animal was bled, 35 ml. in 7 min. from ear vein, equivalent to loss of 20% of blood volume. Systolic pressure in ear artery in mm. Hg. Heart rate in beats per minute.

approximately to only one-third of the initial fall; later the pressure fell again and return to the initial level occupied many hours. The majority of the unanaesthetized rabbits usually showed the first type of recovery curve. A minority showed the second type, and only exceptional animals showed the third. Spontaneous falls and rises of pressure of the order of 30 mm. Hg were common after bleeding but were rare before bleeding when the animals were kept under the standard conditions described.

Heart rate. With the onset of bleeding the heart accelerated rapidly. The increase of rate varied between 20 and 160 beats per min. representing rises of 8–80% over the initial rate of about 200 beats per min. After the haemorrhage

had ceased, the heart rate increased further and reached a maximum about 90 min. after bleeding. The rate then declined slowly, reaching the initial level about 3 hr. after bleeding. Frequently there was a temporary decline of heart rate at the end of bleeding, the fall coinciding with the return of blood pressure. The heart rate soon increased again and the usual prolonged tachycardia was noted. An initial slowing of the heart with the onset of bleeding was never observed.

Anaesthetized rabbits

The first series of animals received 1·4–1·6 g. urethane per kg. intravenously. Corneal and other superficial reflexes were brisk, and deep reflexes very easily elicited. These animals are described as being under 'light' anaesthesia. With

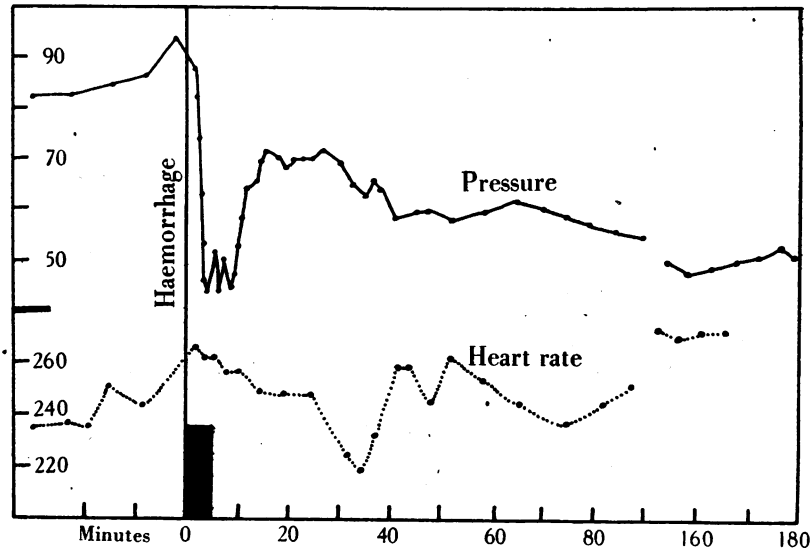

Fig. 2. Pressure changes following loss of 34 ml. of blood in 5 min., equivalent to 26% of blood volume. Urethane, 1·50 g. per kg. body weight injected intravenously 2 hr. before bleeding. Animal killed 5 hr. after bleeding, in good general condition, with ear artery systolic pressure of 45 mm. Hg.

a loss of 23–33% of the blood volume the early changes of systolic pressure and heart rate were similar to those previously described. The animals remained in good condition and reflexes remained brisk until the animals were killed 8 hr. later (Fig. 2).

The second series of animals received 1·64–1·9 g. urethane per kg. intravenously. Superficial reflexes were absent and deep reflexes sluggish. These animals are described as being under 'deep' anaesthesia. With loss of 21–33% of the blood volume, pressure fell sharply to 30–40 mm. Hg. An immediate rise of 20 mm. Hg was followed by a second decline of pressure and death in 1 to 3 hr. (Fig. 3).

Animals of a control series were anaesthetized with similar amounts of urethane. They remained in good condition without marked change of arterial pressure or pulse rate until they were killed 8–10 hr. after induction of anaesthesia.

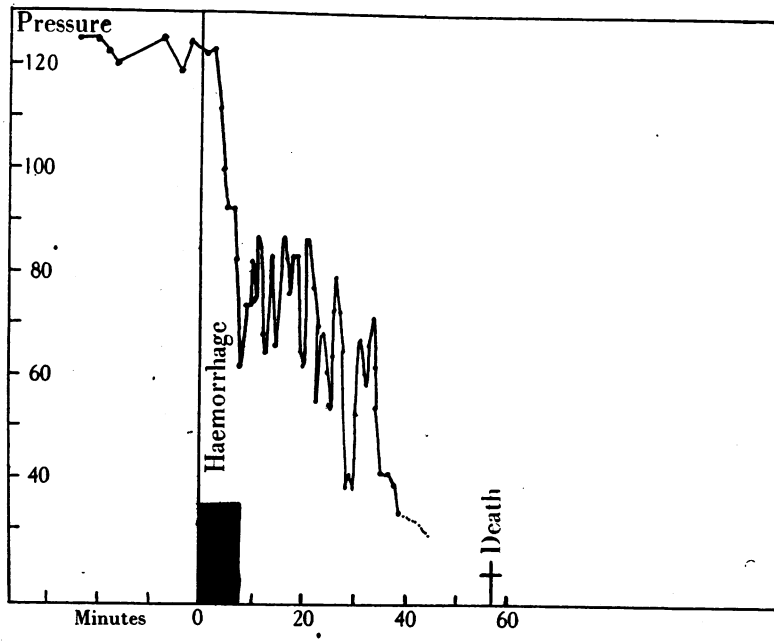

Fig. 3. Pressure changes following loss of 40 ml. in 7 min., equivalent to 26% of blood volume. Urethane, 1·88 g. per kg. body weight, injected intravenously 2 hr. before bleeding. Heart stopped beating 58 min. after venesection.

Dilution of the blood

A few observations were made on the changes of red cell concentration in unanaesthetized and anaesthetized rabbits. Haemoglobin was estimated by the Gowers-Haldane method. Haematocrit values were determined by spinning the blood at 2500 r.p.m. for 45 min. During the bleeding, haemoglobin percentage, red cell count and packed red cell volume fell rapidly. Samples of the issuing blood showed the fall of red cell concentration, and at the end of bleeding the values represented two-thirds of the ultimate change. Following bleeding there was a further decrease of red cell concentration, complete in about 3 hr. These changes were not confined to the issuing blood but were seen in blood samples taken directly from the heart.

These observations confirm the findings of other workers. They show that the blood is 'diluted' rapidly during bleeding and more slowly for about 2–3 hr. after bleeding. It was also confirmed that the coagulation time de-

creased during bleeding. The last drops of blood clotted quickly in the presence of the usual amount of oxalate, and excess of oxalate did not always prevent clotting.

Discussion

The above method of bleeding was used because it was considered that the results would more nearly resemble those seen after free haemorrhage following trauma to a large vessel. The blood loss was limited by the animal's own homoiostatic mechanisms.

Unanaesthetized and 'lightly' anaesthetized rabbits suffer haemorrhage up to one-third of the blood volume without obvious distress. There was no

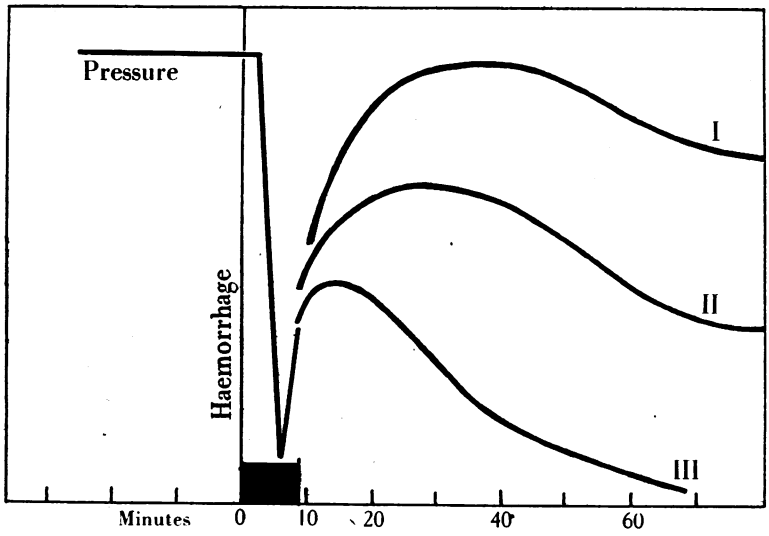

Fig. 4. Diagrammatic summary of the three types of systolic pressure change occurring in the ear artery after haemorrhage.

alteration in diameter of the large vessels of the ears. No unanaesthetized animals died, and 'lightly' anaesthetized animals were in good condition 8 hr. after bleeding. On the other hand, with 'deep' anaesthesia, death occurred in 1–3 hr. after the bleeding. These results show that the injection of different quantities of a non-volatile anaesthetic, such as urethane, may considerably influence the response to bleeding.

The adjustment of the circulation to haemorrhage, expressed in terms of blood pressure, varied in different rabbits. In all instances there was at first little or no change of pressure following venesection. After a latency of 1–3 min. the systolic pressure in the ear artery fell sharply to 30–40 mm. Hg. Thereafter pressure rose quickly, even while bleeding was in progress. The subsequent recovery curves could be differentiated into three types (Fig. 4).

Type 1. Recovery to the initial level. This was complete within 30 min. The high pressure might be maintained or show a small fall after an hour or two.

Type 2. Recovery equivalent to about two-thirds of the initial fall, but a decline again after 40 min. to a lower level. The pressure then rose slowly towards the initial level.

Type 3. A short-lived rise equivalent to about one-third of the initial fall. This recovery was not maintained, pressure falling quickly again to 30–40 mm. Hg. Any later recovery of pressure was very slow.

The consequence of bleeding could be related to the depth of urethane anaesthesia. Unanaesthetized animals usually gave recovery curves of the first type. Animals under 'light' anaesthesia gave curves of the second type, while animals under 'deep' anaesthesia gave curves of the third type. There was some overlap. For example, a minority of unanaesthetized rabbits fitted into type 2, while some 'lightly' anaesthetized animals fitted into type 1. In general one has come to expect the differentiation. The heart-rate changes were of the same order in all animals, irrespective of the pressure changes.

The amount of anaesthetic given was the most constant factor in producing the different types of recovery curves. There was no relation between the amount or rapidity of blood loss and subsequent pressure changes. Equal percentage losses of blood, or approximately equal rates of bleeding, might produce pressure responses of very different types depending upon the presence or absence of anaesthetic.

It is clear that peripheral arterial pressures are not a reliable index of the future of the animal. Rabbits with low pressures appeared just as lively and undistressed as those with fully recovered pressures. Again, it is not possible to account for the different types of response of unanaesthetized animals. It should be emphasized that, since all experiments were carried out under the same conditions, it seems that the differences in response depend upon the physiological characteristics of the animal concerned. Anaesthetics, on the other hand, may upset the normal sequences of the adaptation forces and so alter the blood-pressure recovery.

It would be premature to compare these results with clinical findings because the experiments have been confined to rabbits and only urethane has been used as anaesthetic. Furthermore, the rapid dilution of the blood in the rabbit contrasts with the slow dilution in man.

Summary

1. Unanaesthetized rabbits, and rabbits 'lightly' anaesthetized with urethane, may lose up to one-third of the blood volume by rapid free bleeding from a vein of the ear without distress or deterioration of condition.

2. Animals under 'deep' urethane anaesthesia die 1 to 3 hr. after bleeding.

3. The recovery curves of systolic pressure in the ear artery could be differentiated into three types. The dose of anaesthetic could be related to the type of recovery curve found.

4. Increase of heart rate persisted up to 3 hr. after bleeding and long outlasted the pressure changes.

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