A METHOD OF ARTIFICIAL RESPIRATION FOR CURARIZED MICE

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New drugs possessing a curare-like action have been studied not merely in ordinary conditions but also during artificial respiration [1, 4, 7], because in clinical practice the administration of muscle relaxants is often combined with artificial respiration. Mice are a convenient test object when seeking new drugs and when comparing their efficacy by different pharmacological tests.

For applying artificial respiration the DP-1 apparatus was used. This had several advantages over devices with passive expiration [5], and it has been used successfully in experiments on large animals [2, 6]. Since the switching from the phase of inspiration to expiration and vice versa is regulated in this apparatus by the pressure, and the volume of air inspired by one mouse is very small (0.2-0.5 ml), it was easy to obtain high respiration rats corresponding to the physiological normal for mice (120-220 respirations per minute). The general appearance of the attachment to the DP-1 apparatus permitting artificial respiration to be given to several mice simultaneously, is illustrated in Fig. 1. A system of glass tubes (internal diameter 4.5 mm) with one lead to the DP-1 apparatus and 10 leads connected to metal cannulas, supplies air from the apparatus to the mice during inspiration and in the opposite direction during expiration (Fig. 1B).

After the administration of the first drugs, because of the developing muscle relaxation, the animals could not move and this made it easier to connect them to the artificial respiration apparatus. After introduction of the respiratory tube directly into the trachea, as a result of narrowing of the orifice of the connecting tube (the diameter of the mouse's trachea is 1.2-1.6 mm, the diameter of the intubation tube is 0.5-0.7 mm) the ventilation of the lungs was reduced appreciably, so that it was preferable to introduce the tube directly into the deep portions of the oral cavity (Fig. 2). Having been introduced through the mouth with the tongue drawn forward, the cannula (internal diameter 2 mm, external 4.5 mm) was fixed in the required position by a metal loop behind the upper incisors (Fig. 1A) or by an anchoring ring (Fig. 2). The loop with a metal collar, freely moveable along the cannula, was fixed in the necessary position by a screw. Since the end of the cannula was fixed with a rubber washer and had a conical taper, so that its smaller diameter freely entered the peripharyngeal ring while the larger was too big to do so, when the cannula was pressed in a firm hermetic junction was obtained in the region of the peripharyngeal ring.

However, when the bodies of the mice were in the horizontal position, after insertion of the cannula air from the apparatus entered not only the lungs, but also the stomach, because the orifice of the esophagus is much wider than that of the trachea. To prevent air from entering the stomach, by means of a suitable device the mice were placed on their back with the head thrust forward (see Fig. 1B). It is clear from Fig. 2 that in this case the support beneath the dorsal surface of the neck compressed the tissues and closed the orifice of the esophagus, blocking the pathway to the stomach, as a result of which air from the apparatus during inspiration filled the small part of the pharynx lying next to the cannula and passed along the trachea into the lungs. Technically this method is much simpler than the introduction of an intubation tube into the trachea, and in addition it takes much less time (10-15 sec).

Air entered the lungs by means of an apparatus creating active inspiration and active expiration, so that artificial respiration could be given for several hours during which the activity of the heart remained perfectly satisfactory. The conditions of artificial respiration were as follows: respiration rate 140/min, pressure at inspiration +15 mm Hg, at expiration −10 mm Hg, ratio between durations of phases of inspiration and expiration 1:1. These conditions were optimal and were chosen because with them the pneumogram (recordings were made by means of a carbon pickup, fixed to the chest wall [3] and connected to an ink-writing electrocardiograph), obtainable with curarized mice under artificial respiration, corresponded in frequency, amplitude, and ratio between the duration of the phases of inspiration and expiration to the pneumogram of intact mice at rest. With these working conditions

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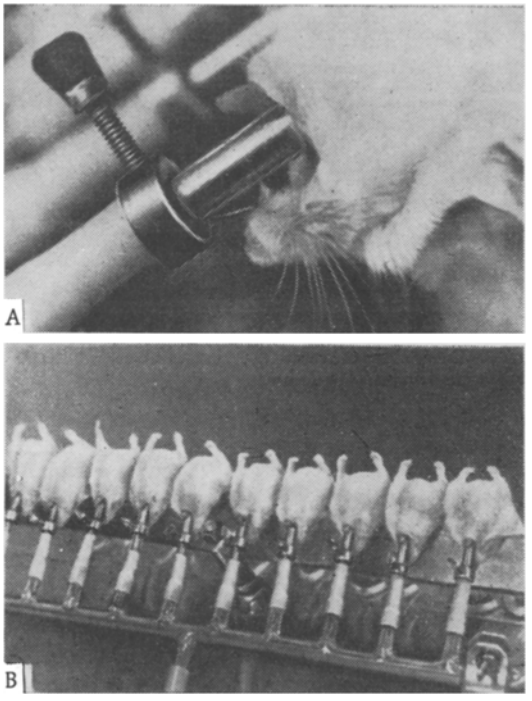

Fig. 1. Attachment to the DP-1 apparatus for giving artificial respiration to several mice at once. A) Fixation of mice behind the upper incisors by means of a metal loop connected to the collar; B) general appearance of the system of tubes for supplying air from the DP-1 apparatus to mice when giving artificial respiration to 10 animals at once.

of the apparatus artificial respiration was fully adequate, as shown by the moderate changes in the blood carbon dioxide tension (pCO_2 before artificial respiration 42±2.9 mm Hg, after artificial respiration for 15 min 35±1.6 mm Hg, after 30 min 29.7± mm Hg), and also by a series of indirect indices: the absence of cyanosis of the skin, maintenance of the cardiac activity for a long period followed by restoration of natural respiration, and the crimson color of the arterial blood at various times in the course of artificial respiration.

To prevent the body temperature from falling during artificial respiration and also to rule out the possibility of changes in the activity of the substances under the influence of variations of temperature, the animals were warmed uniformly and constantly by means of a thermoregulator, switching on a reflector. Without heating the body temperature of the animals fell to 24-26°.

Since the operation of the DP-1 apparatus is possible only if connected hermetically to the animals, and in the process of artificial respiration the inspired air was constantly mixed with the expired, the oxygen and carbon dioxide concentrations were measured by means of a Haldane's apparatus in samples of air taken from the tube during artificial respiration on 10 mice simultaneously after intervals of 3, 5, and 10 min. These measurements showed that the concentrations changed (in the last case the oxygen concentration was 20.4% and the carbon dioxide concentration less than 0.1%). During prolonged work with the apparatus the end tubes were opened for 5 sec every 10 min, thus renewing the air in the tube completely.

More than 1500 experiments have been successfully completed with application of artificial respiration to curarized mice. In experiments performed by this method, if the DP-1 apparatus was worked from an oxygen bag, a 45% oxygen-air mixture was supplied to the mice for artificial respiration, and when working from a compressor, air was supplied. In either case, a certain proportion of inhalational anesthetics could be added.

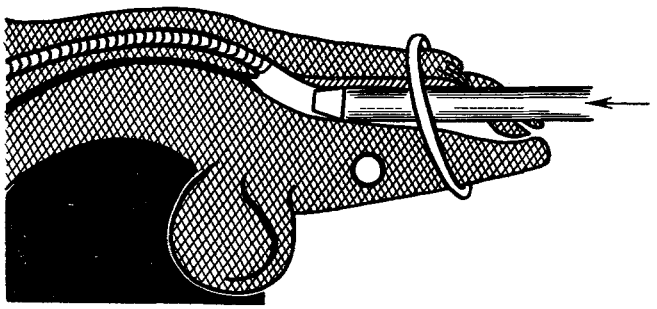

Fig. 2. Position of esophagus and trachea on a schematic section of the head portion of a mouse during application of artificial respiration by means of the attachment to the DP-1 apparatus. The metal cannula is introduced into the deep part of the oral cavity and fixed by an anchoring ring.

LITERATURE CITED

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