Effect of Diffusion Respiration on Duration of Vagal Cardiac Arrest. (20783)

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The always present danger of cardiac arrest during surgical procedures has stimulated a number of investigators within recent years to focus their attention to the etiological factors responsible for this catastrophe(1-4). The effects of anoxia, and more specifically, those of hypercapnia upon vagal cardiac inhibition have received particular attention as causative factors. Studies involving vagal stimulation during hypercapnia suggest that carbon dioxide retention during anesthesia may very greatly augment the effect of any vagal stimulation occurring during operative procedures. However, since previous studies of the effect of hypercapnia on cardiac vagal response have employed stimulation which could not be carefully quantitated, no relationship between the degree of hypercapnia and the duration of cardiac vagal asystole has been reported. The establishment of such an average relationship could well have value in predicting changes in cardiac response to vagal stimulation during respiratory acidosis. Such a correlation is reported in the succeeding paragraphs.

Methods. Since the hypercapnia occurring during a surgical operation is apt to have a gradual onset and is gradually progressive, it was felt desirable in these studies to avoid the precipitous changes in blood pH resulting from the abrupt exposure of animals to high concentrations of carbon dioxide. The method of diffusion respiration(5) was chosen as a means to produce a gradual, but progressive drop in arterial pH. Sixteen adult mongrel dogs of both sexes and varying weights were anesthetized with 35 mg per kg of body weight of sodium pentobarbital. Oxygen was administered endotracheally directly from a cylinder at 2 cm of water pressure through a system having 2 breathing bag reservoirs and a water valve pressure regulator. All of the animals were denitrogenated for one hour prior to the onset of diffusion respiration. During the latter half of the denitrogenation period, control determinations of the duration of vagal cardiac arrest and arterial pH were made. Diffusion respiration was induced in half of the animals by administration of a dose of sodium pentobarbital equal to the initial anesthetizing dose. Respiration was suspended in the second group by the intravenous injection of 0.35 mg per kg of body weight of decamethonium. Electrocardiographic recordings of the duration of vagal cardiac arrest and pH determinations were made at periodic intervals during the experimental period. Stimulation was applied to the right cervical vagus from a thyratron stimulator at 100 cycles per second and a voltage of such an intensity as to produce a minimum duration of cardiac arrest during the control period. This voltage was then used for the remainder of the experiment. The duration of cardiac arrest was determined by standard lead II electrocardiographic tracings. Blood was collected from the femoral artery and the whole blood pH determined by a Beckman glass electrode after allowing 3 minutes for equilibration with room temperature. Since the results are expressed as pH units change in blood reaction, no attempt was made to correct the readings to body temperature.

Results. Upon initiation of diffusion respiration with sodium pentobarbital, the duration vagal cardiac asystole decreased in every instance (Fig. 1). Following this initial decrease, the cardiac vagal response became progressively prolonged, with the response frequently becoming very pronounced at the lower pH levels. In all instances, the duration of cardiac vagal asystole was increased above the control values at the termination of the experiments. Although variability was observed between the behavior of individual animals, a decreased cardiac response to vagal stimulation immediately following the respiratory paralyzing dose of pentobarbital was observed in every experiment. The duration

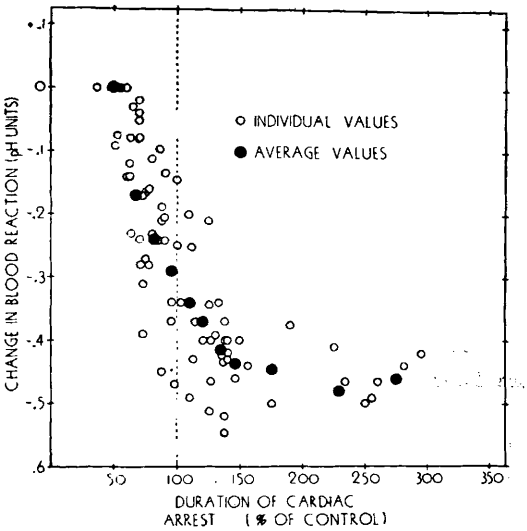

FIG. 1. Effect of respiratory acidosis, caused by diffusion respiration, on duration of vagal cardiac arrest. Diffusion respiration was induced in this series by an overdose of sodium pentobarbital.

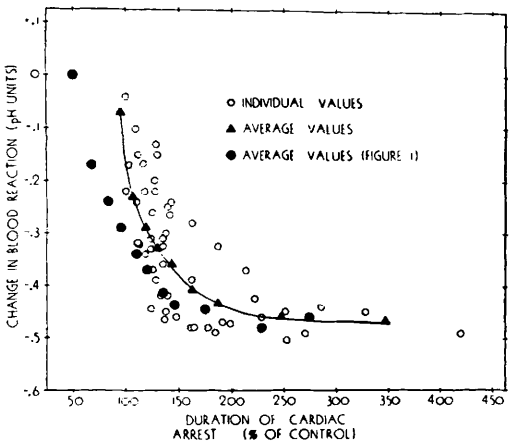

FIG. 2. Effect of respiratory acidosis, caused by diffusion respiration, on duration of vagal cardiac arrest. Diffusion respiration was induced by overdose of decamethonium. Average values from Fig. 1 are superimposed for purposes of comparison of results obtained with pentobarbital and with decamethonium.

of vagal cardiac asystole in this group usually did not return to the control level until the pH of arterial blood dropped in excess of 0.3 pH units.

Since this initially decreased response to vagal stimulation can probably be attributed to the anesthetic(6), a second group of animals was done using decamethonium—a compound which is known to have little effect upon the cardiac vagus(7). In this group, the duration of vagal asystole began increasing gradually from the beginning of the period of diffusion respiration, and became very pronounced at the lower pH levels achieved (Fig. 2).

Discussion. The duration of vagal cardiac arrest in these experiments never became markedly prolonged unless the arterial pH dropped in excess of 0.3 to 0.4 units. Although a paucity of information exists regarding the degree of acidosis which may occur during open chest surgical procedures, Young(4) has reported one case in which the arterial pH of a patient with a tetrology of Fallot dropped 0.3 pH unit during operation. If this could be regarded as an extreme instance(1), and if the above data could be regarded as applicable to the human, it would appear that a pH drop of that magnitude would not have an effect of great importance on vagal cardiac arrest. Such a conclusion seems to be substantially in agreement with investigations of vagovagal reflexes(3) which indicate that only transient cardiac slowing results from stimulation of intact vagal afferent fibers during severe hypercapnia. However, if greater decreases in arterial pH occur, especially in the presence of preexisting cardiac pathology or inadquate oxygenation, vagal mechanisms could well assume a role of some importance in initiating cardiac arrest during thoracic surgery.

Conclusions. 1. Sodium pentobarbital decreases the effect of vagal stimulation on the heart. Hence it is of considerable importance in experiments of this nature to maintain a constant level of barbiturate anesthesia in any one animal. 2. Progressive hypercapnia produced by diffusion respiration causes the duration of vagal cardiac arrest to increase progressively. This increase is very modest with decreases in arterial pH of the magnitude which could be expected in surgical procedures, but becomes especially marked at low pH levels. 3. The probable role of hypercapnia in surgical cardiac arrest is discussed.

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Acquisition of Topical Resistance to Thermal Injury.* (20784)

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Decrease in non-specific inflammatory reaction of tissues repeatedly stimulated by non-living irritating material, has been demonstrated(1-5). In a previous paper(4), we reported that an inflammation, produced by the injection of various irritants into the paw of a rat, protected this paw against a subsequent inflammation. When, after the first local inflammation had subsided, a second generalized hyperergic reaction was produced by an intraperitoneal injection of dextran or egg-white, the characteristic inflammatory edema appeared in the snout, ears and paws, but not in the pre-irritated paw. This permitted us to exclude the direct involvement of higher systemic regulations and to demonstrate this type of protection as being strictly topical.

In the investigation reported here, an attempt was made to obtain some data on the actual state of non-specific "sensitivity" or "reactivity" of pre-irritated tissues to a new inflammatory stimulus. Heat was used for the second irritation and was always given under compression of the blood vessels, thus making the tissues "poikilothermal" and ensuring an absolute uniform irritation in normal and pre-irritated tissues. This procedure eliminated the possibility, existing after a repeated administration of a chemical irritant, that through changes in tissue structures, the irritant might be mechanically prevented from acting uniformly upon the tissues. In this study, the influence of a preceding inflammation on the reaction to "poikilothermal heating" was investigated. The preceding inflammation was induced by the injection of edema-producing irritants, such as dextran or egg-white, into the rat paw, or by rubbing croton oil into the skin of the rabbit ear. Further, the influence of a pre-irritation by poikilothermal heating on the effect of a second, more intense heating was studied. Finally, the problem was investigated as to whether a pre-irritation by heat gives protection also against the reaction to a subsequent irritation by edema-producing chemical irritants.

Methods. Animals: Male Sprague-Dawley rats, weighing between 100 and 120 g, and male albino rabbits of 1.5 to 2.0 kg, were used. *Irritants.* Dextran was given in a saline dilution 1:37.5 of the commercial 6% solution (Macrodex). For local irritation, 0.2 ml was injected beneath the plantar aponeurosis of the hind paw of a rat; generalized hyperergic reaction was produced by the intraperitoneal injection of 1.0 ml. Egg-white was given in a saline dilution 1:5, 0.2 ml for local irritation, 1.0 ml intraperitoneally for generalized reaction. Croton oil, diluted 1:5 with oil (Mazola), was rubbed into the skin of the rabbit ear (2 drops on the upper and 2 drops on the lower surface) using rubber gloves. *"Poikilothermal heating." In rats.* Under compression of the aorta abdominalis with a rubber tube, the right hind paw was placed into 48°C water for 2 minutes, 15 seconds; the compression was then immediately released. For the subsequent irritation (the

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