Laboratory Note

The Goldfish as an Anesthesia and Resuscitation Teaching Model

Mark B. Ravin, M.D.,* and Min K. Tham, Ph.D.†

We have developed an animal model in order to introduce students to the pharmacologic principles of uptake and distribution of drugs, the observation of signs of clinical anesthesia, and the principles of cardiopulmonary resuscitation. We chose goldfish (Carassius auratus) because they are inexpensive, yield reproducible results, and have physiologic traits which make them particularly suitable for demonstrating induction of anesthesia, and because their use as a teaching model makes the demonstration more memorable than when no animal model is used.

There are several reasons why fish may be anesthetized rapidly by bubbling the anesthetic agent into the aquarium: 1) The absence of lungs eliminates functional residual capacity and minimizes deadspace. The gills, therefore, can be thought of as an exposed alveolar-capillary membrane, where gas transport is so rapid that aquatic V A is infinite. 2) The ratio of the flows of blood and water in fish ranges from 1:10 to 1:80, compared with a perfusion-ventilation ratio of 1:2:1 in man. 3) There is a counter-current arrangement of blood-water exchange which continuously exposes the fish blood to a fresh aquatic anesthetic gas source. 4) Fish have a small body size relative to the anesthetic pool to which they are exposed and consequently, the aquatic reservoir of anesthetic is not depleted. 5) The body temperatures of small fish lie within 0.1 C of the water temperature, so temperature solubility gradients are practically eliminated. 6) Studies using electron microscopy have demonstrated that the extracellular space of the goldfish brain appears to be relatively small, and hence anesthetics will rapidly cross the fish blood-brain barrier. 7) Hoar and Cottell found only 0.5 to 1.5 per cent lipid in goldfish. Therefore, we can assume that the Ostwald partition coefficients for goldfish-water would be similar to those for blood-water.

Materials and Methods

Fish approximately 6 months old, 4 to 5 cm in body length, and 2 to 3.5 g in weight, are used. Demonstrations are performed at 28 ± 1.0 C water temperature in 1-liter Pyrex cylindrical beakers. The beakers are filled with water from the aquarium where the fish are stored between experiments. The anesthetic gas bubbling tube is prepared from intravenous tubing. The internal diameter is 3.5 mm. It is sealed at one end and punctured approximately 30 times near the seal with a 26-gauge needle. Although the bubbles rise near the bubbling tube, the movement of the fish creates a turbulent water pattern which distributes the bubbling gas evenly. Thus, the concentration of gas measured approximately 1 cm below the surface is uniform at any sampling site in the beaker.

The fish are placed in the aquarium-beaker one at a time and anesthesia from a gas machine bubbled into the water. With our bubbling tube, a 9 per cent concentration of cyclopropane (200 ml cyclopropane and 2,000 ml oxygen) and a 2 per cent concentration of halothane in oxygen seem optimal. The students, previously informed of the various

* Associate Professor, Department of Anesthesiology.
† Associate in Anesthesiology and Chemical Engineering.

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stages of fish anesthesia, observe and record the progression of anesthetic depths from Stage I through Stage IV. These clinical observations are later correlated with the water anesthetic uptake curves.

Concentrations of cyclopropane and halothane in water are measured by gas chromatography. The 1.0-μl sample is injected directly into the injection port of a Perkin-Elmer model 1900 gas chromatograph equipped with a flame ionization detector. A ½" × 12' column packed with Chromosorb P and moistened with water is used at room temperature. Chromatographic conditions are: injection temperature 100 C; detector temperature 200 C; hydrogen flow rate 40 ml/min, and compressed air flow rate 400 ml/min.

Calculation of concentration is made by comparing the response of the sample with standards. Halothane standard is prepared by dissolving a known weight of halothane in 30 ml water. The cyclopropane standard is a known volume of pure, dry gas injected at room temperature.

Results

STAGES OF ANESTHESIA

Goldfish manifest the following stages of anesthesia when anesthetized with cyclopropane or halothane.

Stage I. As the anesthetic agent is introduced into the aquarium, the fish become agitated, there is an increase in swimming, and the operculum rapidly open and close. This is followed rapidly by a loss of reactivity to external visual and tactile stimuli and by a decrease in the rate of opercular movement. Equilibrium remains normal although there is a loss of muscle tone.

Stage II. Gradually, swimming becomes erratic, with increased opercular rate and reactivity to strong tactile stimuli only. Rapidly, the fish progress to a stage of total loss of muscle tone and equilibrium; opercular movements become very shallow.

Stage III. The fish lie on the bottom of the aquarium; respiration is superficial and irregular. They do not respond to manipulation.

Stage IV. The stage of medullary collapse is characterized by gasping followed by cessation of opercular movement and cardiac arrest. This stage can be maintained for a limited time only without death.

The most important single diagnostic sign is the character of opercular movement. Stages of recovery from anesthesia resemble those observed during induction of anesthesia, but their quantitative delineation is much more difficult.

According to our studies, halothane AD50 for goldfish (half the fish in anesthesia Stage III) occurred at a water concentration of 7 mg/100 ml (0.72 per cent v/v, see Appendix). This value was reached after three minutes of bubbling 2 per cent halothane in oxygen at a flow rate of 2 l/min. This value is in close agreement with the work of others7 who found an AD50 of 7.6 mg/100 ml at 20 C and an AD50 of 9.4 mg/100 ml at 30 C. With 9 per cent cyclopropane, the AD50 of 4 mg/100 ml is reached in 3 minutes when a 2-l/min flow rate is used.

As soon as a fish has passed into Stage IV (respiratory arrest), it is transferred to another beaker containing aquarium water. If the fish is left alone, or the water is gently stirred, there is usually no sign of respiratory movement. However, if the fish is gently compressed between the thumb and forefinger so that water is forced through the gills, it usually recovers.

This demonstration supplants neither our drug uptake and distribution lecture nor the cardiopulmonary resuscitation discussion, demonstration, and practice. Pre- and post-testing indicate that, compared with conventional lecture techniques, the use of the fish model enhances motivation for learning and retention of knowledge.

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References

Circulation

ACIDEMIA IN CYANOTIC INFANTS The author suggests that metabolic acidemia of the newborn secondary to hypoxemia is a common threat to life. The discrepancies between oxygen supply and cellular metabolic requirements for oxygen underlie the problem and form the basis for treatment. The author feels that in infants with cyanotic heart disease, this complication is the most common cause of death.

Once the hypoxic condition occurs, pyruvate arising from glycolysis, which normally should enter into several metabolic reactions (including participation in the formation of acetyl co-enzyme A) is converted anaerobically to lactic acid. Reconversion to pyruvate is the only effective method of reducing lactate levels, and can occur only when systemic oxygen saturations are satisfactory. Only small amounts of lactate undergo renal excretion. During protracted severe hypoxemia, the accumulation of lactate far exceeds the capacity of the tissues to re-oxidize it to pyruvate, resulting in rising accumulations of this potentially lethal substance. Metabolic acidemia can ensue rapidly and demands immediate and vigorous management.

The author describes 30 consecutive infants manifesting acidemia from either cardiac or respiratory causes and discusses frequent monitoring of their blood gases and the use of bicarbonate or THAM-E to help correct acidosis, in addition to the use of palliative and/or corrective surgery for cardiac malformations. (Folger, G. M.: Acidemia of Cardiogenic Origin in Young Infants with Cyanotic Congenital Heart Abnormalities. Clin. Pediatr. 11:573–579, 1972.) ABSTRACTER’S COMMENT: One must take issue with the statement that every effort should be made to return pH to 7.30 and the base excess to no lower than −6 before catheterization or operation is undertaken. In many infants, improvement of acid-base balance will not become evident until after palliative cardiac surgery. Transient metabolic improvement following the administration of exorbitant quantities of sodium bicarbonate or THAM-E is not justifiable when correction or improvement of blood flow (and acidemia) requires surgical intervention.