to be felt before a second was taken. When the ratio was increased from 5 : 1 to 10 : 1, response rate about doubled; when the dose was then increased to 10 mg/kg, the response rate decreased (Table 1). Performance of one rat is shown in Fig. 1.

Nalorphine, a morphine antagonist, temporarily induces an acute abstinence syndrome (*5*). These same four rats, when on a 10 : 1 ratio at 10 mg/kg, were given 4 mg/kg of nalorphine hydrochloride intraperitoneally. Within the next hour, three responded 50 times each, and the fourth, 20 times.

The most interesting aspect of ratio reinforcement was the response pattern after about 2 days on the same ratio and dose. Prolonged periods of no responding alternated with brief periods at a high rate terminated by an injection (Fig. 1*D*). This evidence indicates that the drug was a reinforcer that produced almost immediate satiation.

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3. Details of fabrication and the use of cannula, saddle, and swivel will be included with my reprints, and have also been deposited as Document No. 7304 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D.C. Either a photoprint or 35-mm microfilm copy may be secured by citing the document number and making an advance payment of $1.25 to Photoduplication Service, Library of Congress.
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12 April 1962

Method for Continuous Infusion of Fluids into the Chorioallantoic Circulation of the Chick Embryo

Abstract. A method is described for maintaining long term infusions of fluids into the chorioallantoic circulation of the embryo of the domestic fowl. Infusions can be continued up to 4 days in 6- to 17-day-old chicks, with subsequent hatching.

In order to evaluate the effect of certain substances upon the developing embryo it is often necessary to maintain an effective circulating level during a prolonged, readily controlled interval of time. We have devised a simple method of chronic infusion into the chorioallantoic circulation of the chick embryo. It has been used successfully for the infusion of curare and other neuromuscular blocking agents; pilot studies are now underway utilizing a variety of active substances. Because of the potentially broad applications of this method in embryological research, it is reported here.

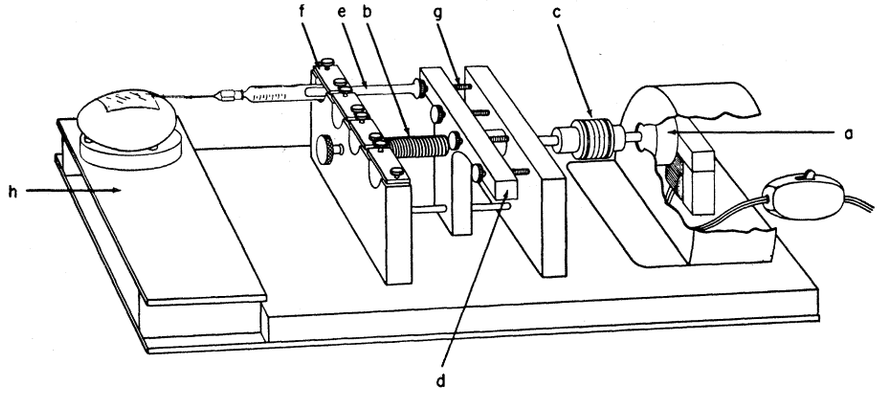

Fig. 1. Diagram of infusion pump in operation.

Essentially, the apparatus consists of a motor-powered multiple syringe drive and glass syringes, coupled to specially shaped microcatheters.

The syringe drive mechanism (Fig. 1) is adapted after Singer (*1, 2*). A synchronous motor (*a*) rotates a drive screw (*b*) coupled via a sylphon bellows (*c*), thus advancing a horizontal bar (*d*) which slowly depresses the syringe plungers (*e*). The syringe barrels are firmly held by clamps (*f*). Plunger adjustment screws (*g*) and an egg platform (*h*) are provided. An infusion rate of approximately 0.01 ml/hr has proved successful with 6- to 17-day-old embryos. We have achieved this rate by using a Telechron 1-rev/hr motor, a drive screw with 40 threads per inch and a 0.5-cm^3 Becton Dickinson tuberculin-type syringe. The rate can be varied by substituting different motors, drive screws, or syringes. Calibration is easily accomplished by allowing the apparatus to run for a given period of time and observing the distance traversed by the syringe plungers.

To prevent leakage of fluid during operation, the syringe plungers and hubs must be coated with high-vacuum grease.

The microcatheter (Fig. 2) is fashioned by hand from No. 10 or No. 20 polyethylene tubing. With moderate practice it can be made in about 3 minutes. The polyethylene is first drawn to a fine taper over a microflame. Two right-angle bends are made by touching the tapered tubing to a warm Nichrome wire controlled by a rheostat. The shaft of the catheter is straightened by contact with the Nichrome heating element. The tip is beveled with a sharp razor blade. Finally, the butt end is flared over a small flame.

Because of certain characteristics of the chorioallantoic circulation, the dimensions of the catheter must be tailored to the age of the embryo to be infused. The chorioallantoic membrane first appears on the 5th day of incubation (*3*). Its blood vessels are sufficiently sturdy to withstand infusion from the 6th day to the 18th or 19th day, at which time the membrane begins to dry out preparatory to hatching. With increasing incubation age, the membrane floats lower beneath the shell and the vessel walls increase in thickness. Thus, the catheter's tip diameter varies from about 200 to 325 μ, the shank length varies from 4 to 8 mm, and the tip length varies from 2.5 to 4 mm at the extremes of the ages used.

The syringe is greased and filled with the injection fluid. A catheter is fitted to the needle tip. Care must be taken to exclude air from the system. The egg is candled, and a Y-shaped chorioallantoic venous (or arterial) bifurcation is located. A rectangular window is removed from the shell and inner shell membrane overlying the selected area. The egg is placed under a dissecting microscope, with the syringe-catheter assembly supported so that the tip overlies the stem of the Y-shaped bifurca-

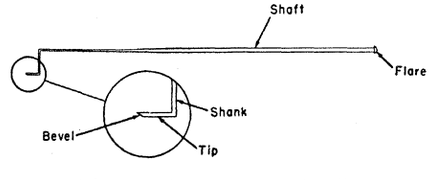

Fig. 2. Microcatheter (detail).

tion. The shank of the catheter is grasped with jeweler's forceps and the tip is first plunged through the chorioallantoic membrane, and is then introduced into the blood vessel from below, in a separate motion. The vessel may be steadied by grasping the membrane with another pair of forceps. Finally, the shaft of the catheter is secured to the egg shell with cellophane tape, and the window is sealed with tape. The egg, catheter, and syringe assembly are mounted on the syringe drive in a standard incubator.

Previously available methods permit short-term injection into or withdrawal of samples from the vascular compartment (*4*). The present technique can be utilized for the short term or long term delivery of a wide range of fluids and particulate suspensions at known rates during given periods of development of the chick embryo. We have infused 6- to 17-day-old incubated embryos at a rate of 0.01 ml per hour for a period of up to 4 days; many of these embryos subsequently hatched successfully.

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19 April 1962

Sodium Iodide Crystal Dosimeters for Use in Surveys of Regions of High Background Radiation

Abstract. In a study of selected regions of high background radiation in Brazil, thallium-activated NaI crystals were used as density amplifiers for dosimeter film badges. Calibration experiments were made, and the field results are summarized.

In a recent survey of background radiation in Brazil (*1*), extensive field use was made for the first time of phosphors as density amplifiers for film badges. While a combination of an ionization chamber and a portable scintillometer can be used to map an external gamma ray field, such a device is needed to integrate the dose received by people as they move through the variable field.

Recently O'Brien, Solon, and Lowder (*2*) have developed the use of a thallium-activated NaI phosphor for low intensity gamma fields with a density amplification of about 1000. A 1⅝- by 2-inch crystal is mounted in a small aluminum can; a small x-ray film (DuPont 508) together with an unopened control film is placed over the crystal, and the can is sealed. Ordinary film badges are sensitive to doses in the order of a fraction of roentgen, but the crystal film pack is sensitive to doses in the order of a fraction of a milliroentgen.

A characteristic feature of the monazite region of Brazil is that the radiation levels vary widely and abruptly. In Guarapari, where most of the measurements were made, the levels vary from a low 10 μr/hr, through street values of 50 to 200 μr/hr, to levels in homes up to 600 μr/hr. Monazite sand spots on the beach can have levels as high as 2 mr/hr, while levels in the monazite plant can reach 5 to 7 mr/hr.

These levels determined two types of procedure in the field and two sets of calibration experiments. For most of the population, the crystal film packs could be carried 24 hours a day. For workers receiving dose rates in the order of 1 mr/hr, the range of levels was first measured with a scintillometer, and the crystal film packs were given to them for periods of an hour or less.

In the first set of calibration experiments, films were exposed for 24 hours in a low background room at different distances from a standard milligram radium source. The background was first measured with an ionization chamber. The spread of the selected doses was slightly broader than those encountered in the city of Guarapari. Data for these calibration experiments are presented in Fig. 1.

In order to interpret the density readings of films exposed for shorter times at higher radiation levels, a second set of calibration films was exposed. In Fig. 2 the data are presented giving lines of constant doses and showing the dependence of density on dose rate.

The field data for the dose rates received by a sample of the populations of the three monazite towns of Guarapari, Meaipe, and Cumuruxatiba are given in summary form in Table 1.

Since this was the first time the crystal film packs had been used extensively in field work, certain precautions were taken. Several repeated

Table 1. Summary of crystal film pack data. Dose rate received by people in monazite sand region, towns of Guarapari, Meaipe, and Cumuruxatiba, Brazil.

Range of dose rate (μr/hr)	Number of persons
> 1000	3
300–1000	3
200– 300	7
100– 200	6
60– 100	7
20– 60	6
10– 20	2

measurements were made. One man working in a low-radiation section of Guarapari was measured on 3 successive days; the results showed levels of 25, 25, and 26 μr/hr, respectively. In a house where the ionization chamber indicated levels from 200 to 230 μr/hr, the married couple were given film packs on 2 successive days. The housewife measured 200 and 205 μr/hr, while the husband, who worked in a bakery with a lower level of radiation, measured 135 and 140 μr/hr. In addition, some film packs were left in locations measured with the ionization

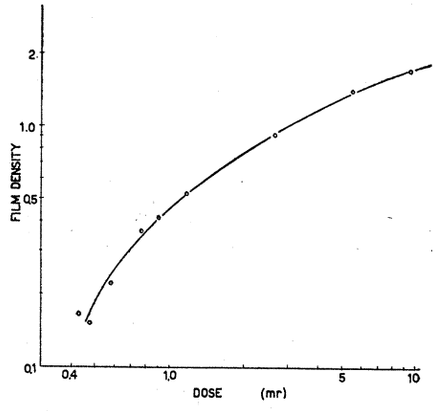

Fig. 1. Film calibration curve for constant time (24 hours), showing dependence on dose.

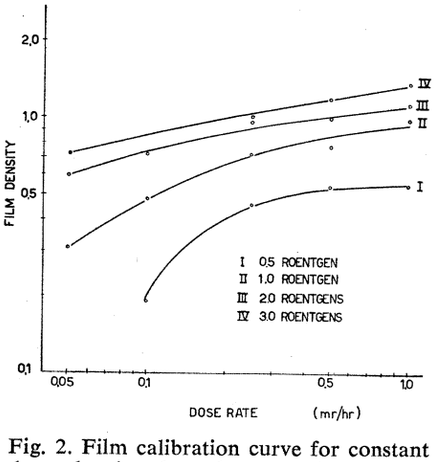

Fig. 2. Film calibration curve for constant dose, showing dependence on dose rate.