

## Laboratory Report

### Brain-Blood Partition Coefficients of $^{85}\text{Krypton}$ at 37 C and 29.5 C

Kathleen Van Horn, B.S.,\* Martin Ingvar, M.K.,† Harvey M. Shapiro, M.D.‡

To permit utilization of the Kety-Schmidt technique for measuring cerebral blood flow during hypothermia, the brain-blood partition coefficients for  $^{85}\text{krypton}$  at 37 C and 29.5 C were determined in a series of cats. At 37 C the partition coefficient for  $^{85}\text{krypton}$  was  $1.092 \pm 0.009$ ; it was  $0.931 \pm 0.007$  (SE) at 29.5 C. These values were significantly different from each other ( $P < .001$ ). (Key words: Solubility, brain-blood partition coefficient; Temperature, solubility coefficient; Hypothermia, solubility coefficient; Gases, nonanesthetic, krypton.)

THE KETY-SCHMIDT METHOD for measuring cerebral blood flow (CBF) requires a knowledge of the brain-blood partition coefficient for the tracer substance used to saturate or desaturate the brain.<sup>1</sup> Numerous studies of the effects of anesthetics on cerebral metabolism and blood flow at normothermia have been conducted with this technique using  $^{85}\text{krypton}$  as the tracer.<sup>2,3</sup> Because the brain-blood partition coefficient for  $^{85}\text{krypton}$  during hypothermia has not previously been reported, we have measured it at 37 C and 29.5 C.

#### Methods

Nine cats (2.5–3.0 kg) were anesthetized with sodium pentobarbital (35 mg/kg, ip) and ventilation controlled with a Harvard venti-

lator connected to a tracheal tube. Catheters were inserted into the femoral artery and vein for blood pressure monitoring, blood sampling, and drug infusions. The muscles and scalp were reflected to permit placement of bilateral trephine holes (~17 mm diameter) in the parietal area. Following dura removal, the muscles and scalp were tightly repositioned with metal clips. Five cats were maintained at 37 C with an infrared heat lamp connected to a temperature controller receiving its input from a rectal thermal probe. Four cats were surface cooled to 29.5 C and maintained at that temperature for 90 minutes prior to determining the  $^{85}\text{krypton}$  partition coefficient.

The animals were ventilated with a mixture of  $^{85}\text{krypton}$  in oxygen (0.5 mCi/l). Equilibration times were 45 minutes for animals maintained at 37 C and 90 minutes for those at 29.5 C. Previous unreported studies in our laboratory showed that cerebral arteriovenous differences for  $^{85}\text{krypton}$ , after 45 minutes of ventilation with the same  $^{85}\text{krypton}$ -oxygen mixture, were less than 2 per cent at 29.5 C. The respiratory rate was chosen to achieve a  $\text{Paco}_2$  of 65–75 torr to further facilitate full equilibration between the brain and blood.

Arterial blood (0.5 ml) was anaerobically sampled via a manifold system with a calibrated Hamilton syringe and delivered through a 19-gauge needle into the bottom of a pre-weighed scintillation vial containing 20 ml of scintillation counting medium.<sup>4</sup> The vials were quickly sealed with gas-tight caps, shaken, reweighed, and centrifuged prior to being counted in a liquid scintillation counter.

Brain sampling was accomplished with a 10-ml plastic syringe with its end cut off and the exposed edges sharpened.<sup>1</sup> This sampling syringe was driven between the previously established trephine holes immediately after the animal was killed with saturated potassium chloride. A cork, placed on the side opposite the syringe-entry trephination site,

\* Research Assistant.

† Medical Student, University of Lund, Lund, Sweden.

‡ Associate Professor of Anesthesia and Neurosurgery.

Received from the Department of Anesthesia, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania 19104. Accepted for publication January 25, 1976. Supported in part by USPHS Research Center Grant 5-P01-GM-15430-07, and Research Training Grant 5-T01-GM-00215-16, from the National Institute of General Medical Sciences, National Institutes of Health.

Address reprint requests to Dr. Shapiro at his present address: Anesthesia Research Laboratory, Veteran's Administration Hospital, 3350 La Jolla Village Drive, San Diego, California 92161.

was used to provide a base against which the sampling syringe was driven and to seal the syringe before it emerged into the air. The plugged syringe was then withdrawn, and the plug quickly exchanged for a tightly fitting rubber stopper. The replacement stopper was connected to a stopcock on which was mounted a 5-ml glass syringe and 2-inch 19-gauge needle. The deadspace in this system had previously been filled with water equilibrated with the <sup>85</sup>krypton-oxygen breathing mixture. The brain sample was then flushed back and forth between the plastic sampling syringe and the 5-ml glass syringe to effect homogenization. Following this, the sample was introduced into the scintillation vials in the same manner as was done for the blood. A scintillation brain blank was prepared from a separate animal. Counting efficiencies were determined with external standards and were approximately 75 per cent for blood and 80 per cent for brain.

The brain-blood partition coefficient was calculated by the following formula:

$$S = \frac{C_{\text{brain}}}{C_{\text{blood}}}$$

Where S = partition coefficient;  $C_{\text{brain}}$  = concentration of <sup>85</sup>krypton/gram of brain (includes tissue and blood contained therein);  $C_{\text{blood}}$  = <sup>85</sup>krypton concentration/gram of blood at equilibration.

## Results and Discussion

The results are summarized in table 1. They indicate that hypothermia to 29.5 C significantly ( $P < .001$ ) lowers the brain-blood partition coefficient for <sup>85</sup>krypton. Our normothermic value for S of 1.092 showed a small, but significant, difference ( $P < .05$ ) from a previously reported value of 1.059.<sup>2</sup> The pres-

TABLE 1. Brain-Blood Partition Coefficients (S) for Cats at 37 C and 29.5 C (Mean  $\pm$  SE)\*

	37 C	29.5 C
Cat 1	1.081	0.941
Cat 2	1.079	0.921
Cat 3	1.075	0.944
Cat 4	1.107	0.917
Cat 5	1.120	—
AVERAGE	1.092	0.931
SE	0.009	0.007

\* Five cats were studied at 37 C, four additional cats at 29.5 C.

ent study is in agreement with recently reported results indicating a significant alteration by similar hypothermia of the partition coefficient of another tracer employed in the measurement of CBF (<sup>133</sup>xenon).<sup>3</sup> The effects of temperature on the partition coefficients of tracer substances used to determine CBF should be considered when these measurements are performed.

## References

1. Kety SS, Harmel MA, Broomell HT: The solubility of nitrous oxide in blood and brain. *J Biol Chem* 173:487-496, 1948
2. Lassen NA, Munck O: The cerebral blood flow in man determined by the use of radioactive krypton. *Acta Physiol Scand* 33:30-49, 1955
3. Smith AL, Wollman H: Cerebral blood flow and metabolism. *ANESTHESIOLOGY* 36:378-400, 1972
4. Smith AL, Thomas JW, Wollman H: Determination of the concentration of volatile isotopes in blood by liquid scintillation counting. *Int J Appl Radiat Isot* 21:171-174, 1970
5. Hagerdal M, Harp J, Nilsson L, et al: The effect of induced hypothermia upon oxygen consumption in the rat brain. *J Neurochem* 24:311-316, 1975