ANOMALOUS CONCENTRATION GRADIENT IN NaI SOLUTIONS INADVERTENTLY FROZEN IN TRANSIT

To the Editor: Therapeutic doses of iodine-131 (^{131}I) are frequently dispensed volumetrically from a stock vial containing a solution of sodium iodide. During the winter months we have observed that initial aliquots do not always have the same radioactive concentration as that calculated for the bulk solution. Accurate radioactive dispensing on a volume basis requires that the stock vial be subjected to mixing following delivery.

In order to evaluate the cause and extent of this problem, we prepared a stock solution of low radioactive concentration sodium iodide with the same concentration of sodium thiosulfate (0.2% wt/vol) and pH (7.0–8.5) as that in the stock therapeutic iodine vial. Fifteen-milliliter aliquots of this solution were transferred to plastic tubes and were stored at various temperatures (ambient, 6°C, −5°C, −10°C, −15°C, and −30°C). Temperatures below zero were maintained by immersion of the tube in a thermostatically controlled cooling bath. At temperatures above zero, the tubes were stored undisturbed for six days prior to analysis. Those samples stored below zero, but which did not freeze, were stored for 24 hr prior to analysis. Frozen samples were allowed to thaw overnight at 6°C prior to analysis except where otherwise indicated. In addition, the −30°C samples were either rapidly frozen (tubes plunged into the cold bath at −30°C) or slowly frozen (tubes allowed to cool down with the cold bath from ambient temperature to −30°C). In order to evaluate whether or not the gradient developed during the process of freezing or thawing, three tubes frozen at −30°C were sectioned while still frozen. The volumes of all samples (~1 ml) were accurately established by weight. The results are reported as a ratio of the radioactive concentration (activity/gram) of the sample to that of the untreated solution. The results reported in Table 1 are for those samples which did not freeze. These results clearly show that no concentration gradient developed in any case where the samples did not freeze. However, once the sample froze and subsequently thawed, a significant concentration gradient developed (Fig. 1). Throughtout the majority of the upper portion of the tube, this concentration gradient was remarkably constant irrespective of the temperature at which the sample was frozen. However, at the very base of the tube, the concentration of the sample frozen at −10°C, (i.e. the sample right on the freezing point of the solution) showed a marked increase. The samples frozen at −15°C and then thawed at 6°C and analyzed immediately were identical to those frozen at −15°C and allowed to thaw and stand at 6°C overnight. This indicated that at 6°C little appreciable mixing by diffusion occurred overnight. The results from the samples frozen at −30°C, rapidly frozen or slowly frozen, and thawed (Fig. 2) clearly indicate that, although tubes subjected to the slower freezing appear to form a somewhat more uniform concentration gradient, there was no practical difference in the slope of concentration gradients developed. However, the sample frozen at −30°C

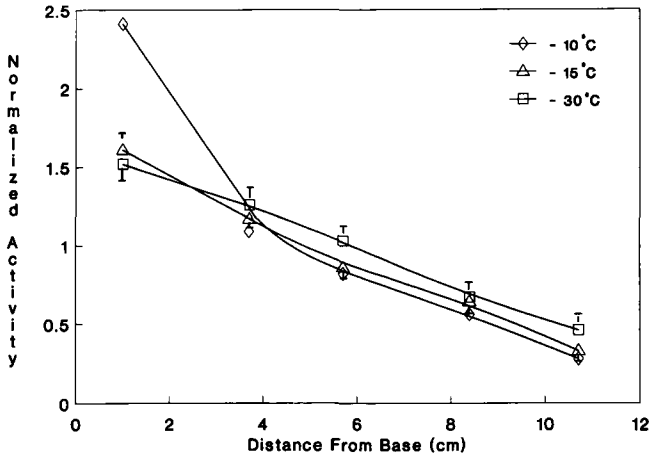

FIG. 1. Radioactive concentrations of aliquots from samples frozen at −10°C (◇), −15°C (△), and −30°C (□) and thawed at 6°C, as a function of the distance from the bottom of the tube. Data are given as the mean ± s. d. (n = 3).

TABLE 1. Radioactive Concentration *versus* Sample Depth in Unfrozen Tubes

Temperature °C		Distance of Sample From Bottom of Tube (cm) 1.0	3.7	5.7	8.3	10.7
22	$\bar{x}$	1.01	1.00	1.01	1.01	1.03
	±	0.03	0.02	0.02	0.03	0.09
6	$\bar{x}$	1.03	1.03	1.00	1.03	1.02
	±	0.02	0.02	0.02	0.02	0.02
0	$\bar{x}$	1.10	1.01	1.01	1.01	0.99
	±	0.02	0.02	0.02	0.02	0.02
−5	$\bar{x}$	0.99	0.99	0.97	0.97	0.97
	±	0.02	0.02	0.02	0.02	0.02
−10	$\bar{x}$	1.00	1.06	1.01	1.01	1.05
	±	0.02	0.02	0.02	0.02	0.02

All values are the mean and standard deviation of 3 samples except −10°C where one sample froze (see Fig. 1).

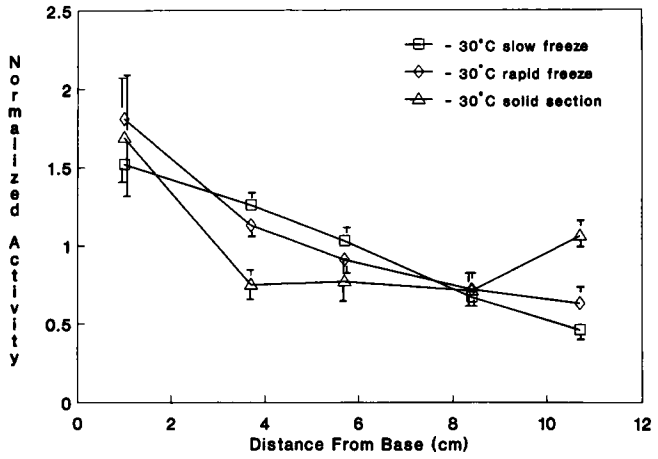

FIG. 2. Radioactive concentration of aliquots from samples rapidly frozen (◇) or slowly frozen (□) at −30°C and thawed at 6°C, or rapidly frozen but sectioned while still frozen (△), as a function of the distance from the bottom of the tube. Data are given as the mean ± s. d. (n = 3).

and sectioned while frozen showed a significantly different concentration profile from the thawed samples, in that elevated concentrations were observed at both the top and bottom of the tube.

One possible physical explanation for the development of these concentration gradients is that the initial freezing occurred on the walls of the tube, predominantly in the central region. The liquid portion would become enriched in radioactivity relative to the frozen portion due to depression of the liquid freezing point by the sodium thiosulfate and sodium iodide and the consequent tendency for the frozen portion of the mixture to have a lower concentration of solute. If the central region froze ahead of either of the end sections, the liquid body would be divided into two, trapping the higher radioactive concentrations at either end as final solidification occured. Conversely, during thawing, the depression of the freezing point due to increased salt concentration would lead to the areas of greater radioactive concentration melting first. The low thermal conductivity of the frozen sample would cause the sample at the sides of the tube to thaw first. This would allow the solidified material to float and displace the melted material downward. The high salt concentration in the lower portions of the tube would then be reinforced. The end result would be the development of a linear concentration gradient over the majority of the tube. The very sharp increase in radioactive concentration at the bottom of the tube frozen at −10°C (Fig. 1) may relate to the slower rate of freezing that would occur right at the freezing point. This would allow an even lower salt concentration to develop in the initial solid material with a concomitant increased salt concentration in the last material to solidify.

These results clearly show that when there is a risk of freezing during transportation of therapeutic solutions of sodium iodide it is essential to physically mix the liquid once thawing is complete if therapeutic doses are to be dispensed accurately on a volume basis.

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