Suppression by Perchlorate of Technetium-99m and Iodine-123 Secretion in Milk of Lactating Goats

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Lactating goats were infused with either technetium-99m (^{99m}Tc) or iodine-123 (^{123}I) together with chlorine-36 (^{36}Cl) through an indwelling catheter previously placed in an external pudic mammary artery. The radioisotope infusions were repeated together with 100 mg of sodium perchlorate. There was a rapid transfer of ^{99m}Tc and ^{123}I into milk, reaching a peak concentration 30 min after a 15-min infusion. The fractional secretion of ^{99m}Tc and ^{123}I in milk was reduced by 70%–80% and 60%–66%, respectively, by perchlorate. The fractional secretion of ^{36}Cl was not affected by perchlorate, and the shape of the ^{36}Cl secretion curve differed from those of ^{99m}Tc and ^{123}I, which were similar. It is probable, therefore, that the latter nuclides were secreted by a transport route different from that of chloride. Available data describing the secretion of ^{99m}Tc in human milk after pertechnetate administration was reviewed, and it was concluded that perchlorate pretreatment significantly reduced the secretion of ^{99m}Tc in human breast milk.

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Administration of a radiopharmaceutical to a lactating mother will result in secretion of radioactivity in breast milk. Of the ^{99m}Tc radiopharmaceuticals whose secretion has been investigated, the greatest magnitude and widest range in fractional secretion of radioactivity into milk is produced by administration of [^{99m}Tc] pertechnetate (*1–3*). The secretion of ^{99m}Tc in human breast milk has been studied following both pertechnetate brain scans and pertechnetate thyroid scans. Inspection of these data shows a greater concentration of activity in milk after thyroid scans compared with brain scans (*3*). It has been suggested that a cause of this difference is the pretreatment of the latter patients with potassium perchlorate (*3*), which is given to reduce the uptake of pertechnetate by the choroid plexus and by the thyroid gland. In many respects, perchlorate, pertechnetate, and iodide have similar effects in vivo. For instance, both pertechnetate and perchlorate will act as competitive inhibitors of iodide uptake by the thyroid gland (*4*), and perchlorate will suppress the secretion of radioiodide in milk of rabbits and cows (*5–7*). However, there are no data to describe the effect of perchlorate on ^{99m}Tc secretion in milk.

The purpose of this report is to describe such an investigation on lactating goats that had been especially prepared for mammary gland transport studies (*8*). For comparison, the study was repeated using sodium [^{123}I] iodide, and in both studies, ^{36}Cl was administered simultaneously to compare the ^{99m}Tc and ^{123}I transfer with another halogen that has a well characterized transport mechanism (*9*).

MATERIALS AND METHODS

The goats were prepared by implanting a polyvinylchloride catheter in an external pudic mammary artery, as described previously by Fleet and Mepham (*8*). This technique allows continuous infusion of labeled compounds directly into the arterial blood supply to the mammary gland (close-arterial infusion).

Goat A was infused continuously for 30 min with 17 ml saline immediately followed by a 15-min infusion of sodium [^{99m}Tc]pertechnetate* (2.8 MBq) and sodium [^{36}Cl]chloride* (0.1 MBq). The same solutions were infused into goat B with 100 mg sodium perchlorate,† also administered at a constant

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rate during the 45-min infusion. The following day, goat A was infused as above with perchlorate and goat B without perchlorate. The $^{123}I^{\ddagger}$ infusions (2.8 MBq) were conducted as above, except that the perchlorate was administered to both animals on the second day (goats B and C).

Milk was expressed completely at 15-min intervals from the infused glands immediately after 150 mU oxytocin i.v., starting 30 min before the isotope infusion to give three background measurements, and continuing for 2 hr beyond initiation of the isotope infusion. The total amounts of ^{99m}Tc and ^{36}Cl infused and the total amounts secreted in 2 hr were determined from counting samples of the infusate and samples of the milk, and correcting for decay to the start of the isotope infusion. For the ^{99m}Tc and ^{123}I infusions without perchlorate, the distribution of ^{99m}Tc and ^{123}I in milk between fat, aqueous phase, and casein was determined by high-speed centrifugation of the milk sample from goat B, which had the maximum concentration of these isotopes (*10*).

TABLE 1
Fractional Secretion of ^{99m}Tc, ^{123}I, and ^{36}Cl Activities and Milk Yield Produced With and Without Perchlorate During the 2-hr Period After Initiation of a 15-min Close-Arterial Infusion

		Fractional secretion (%)			
Goat	Perchlorate	^{99m}Tc	^{123}I	^{36}Cl	Yield (ml)
A	With	0.4		0.6	117
	Without	1.3		0.6	138
B	With	0.3		0.4	132
	Without	1.6		0.5	145
B	With		0.5	0.5	191
	Without		1.5	0.7	187
C	With		0.4	0.4	150
	Without		1.0	0.4	115

RESULTS

Technetium-99m Infusions

The variation of the concentration of ^{99m}Tc with time was calculated as a percentage of the infused activity (Fig. 1), and the total fractions of activity secreted during the 2-hr collection period are given in Table 1. No ^{99m}Tc was detected above background in the milk before initiation of the second day's infusions. Without perchlorate, there was a rapid increase in the activity concentration, reaching a maximum at 30 min after starting the infusion. When perchlorate was administered, the maximum activity concentration was greatly reduced and there was a slower decrease in the activity concentration beyond the peak value, which also occurred at 30 min. Administration of perchlorate resulted in a reduction of 70% and 80% in the total fractional activity of ^{99m}Tc secreted in 2 hr by goats A and B, respectively. In the milk sample removed from goat B 30 min after initiation of the infusion, 87% of the ^{99m}Tc was in the aqueous, 11% was in the casein, and 2% was in the fat phase.

The concentration of ^{36}Cl measured in the milk before starting the second day's infusions was about 5% of the subsequent peak value and was assumed to be constant during the course of the 2-hr collection period. The background-corrected time-activity curve for ^{36}Cl secretion reached plateau values at 30 min after initiation of the isotope infusion and followed a different

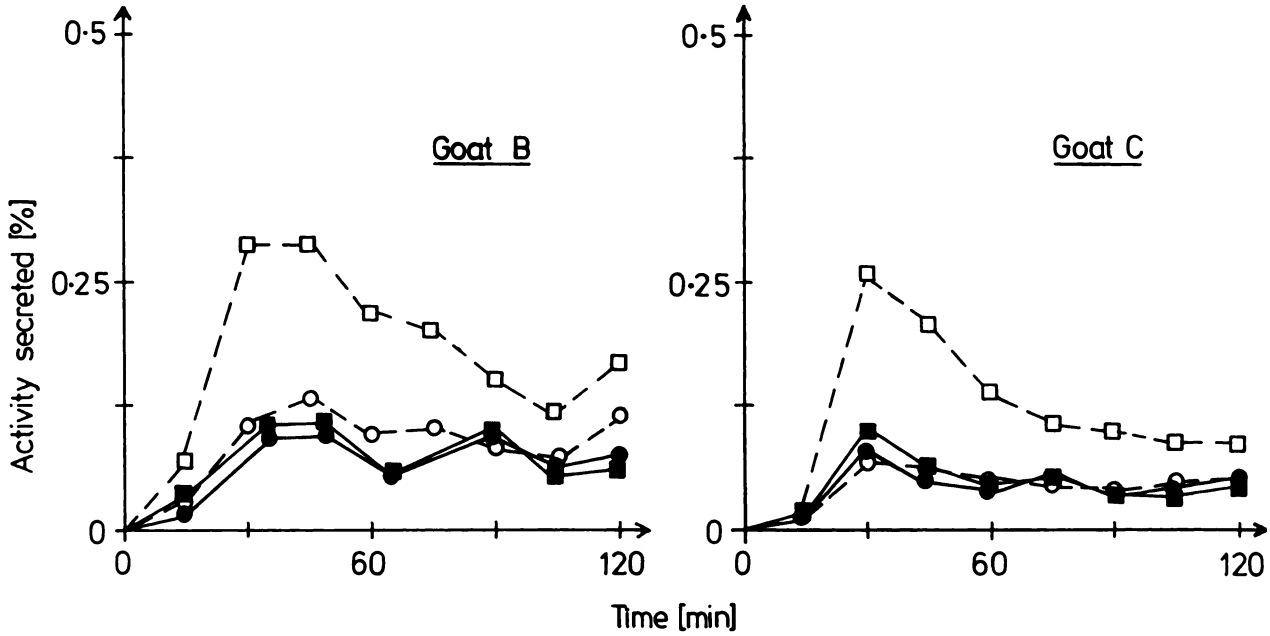

FIGURE 1
Secretion in milk from goats A and B of ^{99m}Tc without perchlorate (□– – –□), ^{99m}Tc with perchlorate (■——■), ^{36}Cl without perchlorate (○– – –○) and ^{36}Cl with perchlorate (●——●).

pattern from the ^{99m}Tc curves (Fig. 1). The fractional secretion of ^{36}Cl without perchlorate was considerably less than ^{99m}Tc (Table 1). Perchlorate had no effect on the pattern of secretion or the fractional secretion of ^{36}Cl in milk. Perchlorate also had no effect on the milk yield during the 2-hr collection period (Table 1).

Iodine-123 Infusions

There was a significant concentration of ^{123}I in the three preinfusion milk samples taken on the second day. These activity concentrations decreased at a rate of 20% per 15-min interval. The subsequent measured ^{123}I activities were corrected with a background curve extrapolated from the preinfusion activities to decrease exponentially at this rate. The ^{36}Cl background on the second day was treated as before.

The background corrected variation in the concentration of ^{123}I and the total fractional secretions were similar to that of ^{99m}Tc (Fig. 2 and Table 1). Perchlorate produced the same effect on the shape of the secretion curve as ^{99m}Tc, and produced a decrease in the fractional ^{123}I excretion of 67% and 60% in goats B and C, respectively. The distribution of ^{123}I in milk removed from goat B 30 min after initiation of infusion was 91% in the aqueous, 5% in the casein, and 4% in the fat phase. The pattern and magnitude of ^{36}Cl secreted in milk were similar to that measured during the ^{99m}Tc experiments (Fig. 2 and Table 1).

DISCUSSION

A very similar pattern and magnitude of secretion in goats' milk was demonstrated between [^{123}I]iodide and [^{99m}Tc]pertechnetate with peak activity occurring 30 min after initiation of a 15-min continuous infusion (Figs. 1 and 2). Previous work has shown that the secretion of radioiodide in the milk of rabbits and cows is suppressed by perchlorate or other competing anions (*5–7*). The present study has confirmed earlier work and has also shown that the secretion of ^{99m}Tc in goats milk can be inhibited by perchlorate. The similarity in the effect of perchlorate on ^{123}I and ^{99m}Tc secretion in milk, and the known reduction of ^{99m}Tc and ^{123}I thyroid uptake by perchlorate, suggests a close similarity between the trapping mechanism in the mammary gland and in the thyroid. This study has also shown that ^{36}Cl has a different pattern of secretion from ^{123}I and ^{99m}Tc, and that ^{36}Cl transfer is not affected by perchlorate (*9*).

The slower decrease in activity concentration of both ^{99m}Tc and ^{123}I with perchlorate administration may have been due to the latter having been infused continuously for 30 min before starting the isotope infusion, thereby, ensuring that any perchlorate-induced inhibition was established before the start. However, the slower decrease may have been due to the fact that the kinetics of [^{99m}Tc]pertechnetate transfer from blood into milk is altered by perchlorate pretreatment (*11*). The similar pattern of results for goats A and B in the ^{99m}Tc infusion experiment on consecutive days indicated that there was little retention of perchlorate inhibition 24 hr after administration. The slightly greater perchlorate suppression of ^{99m}Tc secretion compared with ^{123}I secretion may have been due to such factors as the greater milk production in the ^{123}I infusions (Table 1, goat B), different quantities of carrier nuclides,

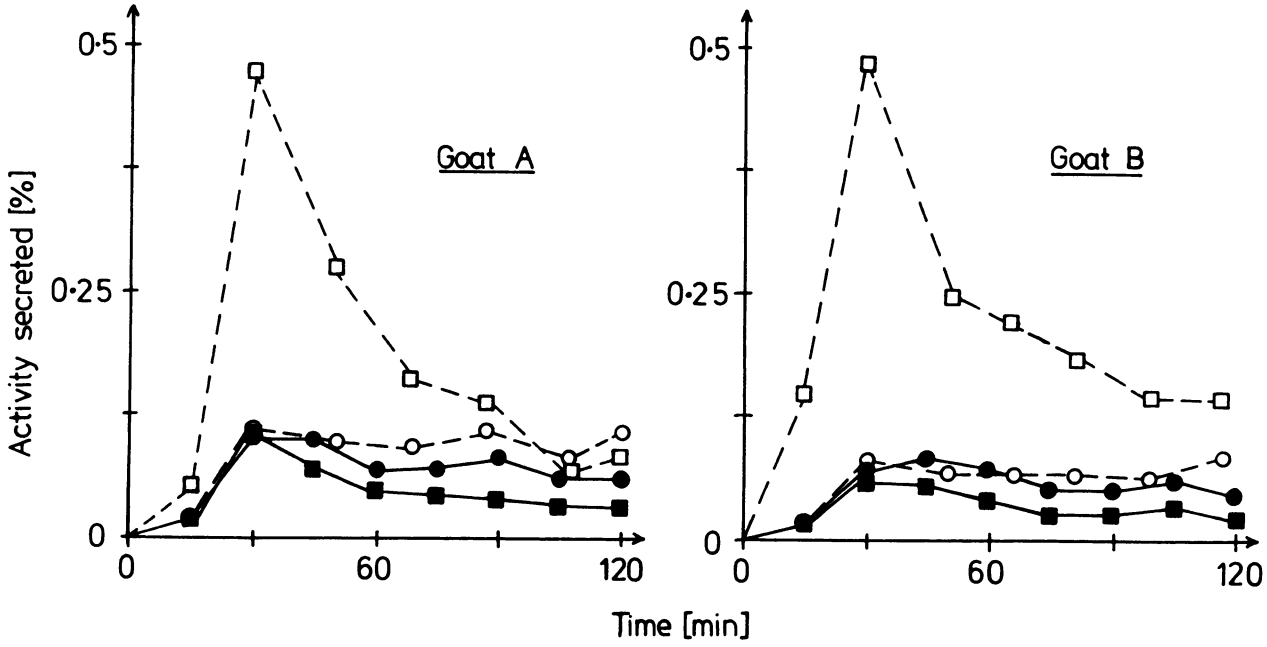

FIGURE 2
Secretion in milk from goats B and C of ^{123}I without perchlorate (□– – –□), ^{123}I with perchlorate (■——■), ^{36}Cl without perchlorate (○– – –○) and ^{36}Cl with perchlorate (●——●).

or genuine quantitative differences between the perchlorate inhibition of ^{99m}Tc and ^{123}I secretion.

The ability of perchlorate to suppress ^{99m}Tc and radioiodide secretion in milk raises two questions. First, could perchlorate be administered to lactating mothers with other ^{99m}Tc compounds (such as [^{99m}Tc]macroaggregated albumin) or iodinated compounds, which yield large secretions in milk, in order to minimize the radiologic hazard to the infant (*1–3*)? Second, could perchlorate be administered to cows and goats immediately after the appearance of fission product fallout following a Chernobyl-type incident, in order to reduce the radioiodide content of milk destined for human consumption (*12,13*)?

To answer these questions, perchlorate secretion in milk must be quantified. We have failed to identify any published data describing the secretion of perchlorate in milk. It has been found that thiocyanate suppressed radioiodide secretion in rabbit milk without concentration of the inhibiting anion in milk (*5,6*). If this is also true for perchlorate, then the conditions for total saturation of the mammary gland transport mechanism must be investigated.

The present studies in goats provide direct evidence for the inhibition of [^{99m}Tc]pertechnetate transfer from blood into milk by perchlorate. Table 2 summarizes the concentration of ^{99m}Tc in human breast milk 3 hr after injection of pertechnetate (*14–20*). These values were either experimental measurements or were taken from exponential curves fitted to the secretion data, and they have been grouped according to the additional administration of perchlorate. None of these published reports were derived from subjects with abnormal thyroid gland activity or thyroid medication. Activity concentrations fell into a low range (1.2×10^{-3} to 2.8×10^{-3}%/ml milk) with perchlorate administration and a high range (4.5×10^{-3} - 1.0%/ml milk) without perchlorate administration (Table 2). These results are consistent with the direct measurements made in goats indicating that perchlorate causes lower secretion of ^{99m}Tc into milk, in both species. Thus, the appropriate period for interrupting breast feeding after pertechnetate administration may be reduced for radiologic reasons if perchlorate is also administered. However, assessment of perchlorate secretion is essential before this procedure could be routinely recommended, in case such secretion would warrant an interruption for pharmacologic reasons. The findings also emphasize the urgent need to find alternative, and more acceptable inhibitors.

TABLE 2
Concentrations of ^{99m}Tc in Human Breast Milk 3 hr After Injection of Pertechnetate, Expressed as a Percentage of the Injected Activity

Perchlorate	Scan	Activity concentration (%/ml milk)	(Ref.)
With	Brain	1.2×10^{-3}	(*14*)
	Brain	2.4×10^{-3}	(*15*)*
	Brain	2.8×10^{-3}	(*15*)*
Without	Brain	4.5×10^{-3}	(*16,17*)
	Thyroid	1.0×10^{-2}	(*18*)
	Thyroid	2.2×10^{-2}	(*20*)
	Thyroid	4.5×10^{-2}	(*1*)
	Thyroid	5.3×10^{-1}	(*19*)
	Thyroid	1.0	(*19*)

* Also, Wyburn JR, personal communication.

NOTES

* Amersham International plc, U.K.
† Macarthys Ltd., Romford, U.K.
‡ AERE, Harwell, U.K.

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