

# CLINICAL SCIENCES

## INVESTIGATIVE NUCLEAR MEDICINE

### Kinetics of the Human Thyroid Trap: A Compartmental Model

Marguerite T. Hays

*Veterans Administration Hospitals, Buffalo, New York, Washington, D.C.,  
and Veterans Administration Central Office, Washington, D.C.*

*Thyroidal pertechnetate was measured continuously in normal subjects for 40 min after i.v. injection, using a multicrystal camera. Digital counts (1-min increments) were read directly from the magnetic tape and summed for the thyroidal area and for adjacent neck background. The net thyroidal data were used as the basis for development of a compartmental model of the thyroidal trap, using the SAAM program. Input to the trap in the model is plasma pertechnetate radioactivity, measured frequently during the study and fitted to a multiexponential equation. Best fit of the thyroidal data was achieved with a model in which the trap is described by two compartments, a fast ("follicular cell") compartment and a slower ("colloid") compartment. Iodide blockade, administered either during the study or 1 hr before its initiation, rapidly blocked the trap at the point of input from plasma into the follicular cells. Iodide did not affect the other parameters of the model.*

J Nucl Med 19: 789-795, 1978

Radioiodine studies of the thyroid's iodide-concentrating mechanism (the "trap") in man are usually complicated by the presence of large quantities of organically bound tracer. Only in certain disease states, or after complete medicinal blockade of iodide organification, does study of radioiodine concentration give specific information about the trap. There is no *a priori* reason to believe that the trap is normal in such states. Use of an agent that "discharges" the trap by competitively inhibiting iodide concentration is helpful in determining the size of the trap at a given time, but nothing about trap kinetics can be learned from such a study.

When [ $^{99m}\text{Tc}$ ] pertechnetate ( $^{99m}\text{TcO}_4^-$ ) became available, it was quickly identified as an agent that became concentrated in the same tissues that concentrate iodide (1). Since it does not participate in thyroid hormone formation, it was suggested as a model for the iodide trap. Certain problems, however, have limited the usefulness of  $^{99m}\text{TcO}_4^-$  for this purpose:

1. While experimental results have been contradictory (2-6), it appears that, at least under certain

circumstances, organic binding of  $^{99m}\text{TcO}_4^-$  to the thyroid occurs.

2. In vitro studies have demonstrated that the  $K_m$  of  $\text{TcO}_4^-$  transport into thyroid slices differs from that of iodide (7). This, together with demonstration of significant plasma binding of  $^{99m}\text{TcO}_4^-$  (8), indicates that results of kinetic studies of  $^{99m}\text{TcO}_4^-$  uptake cannot literally be translated to the iodide situation.

3. Except when the trap is stimulated, concentration of  $^{99m}\text{TcO}_4^-$  in the normal thyroid is often less than double the concentration in surrounding neck tissues. When the usual type of thyroidal uptake equipment is used, the neck background is so great that the normal trap may be impossible to distinguish from a suppressed trap (9). Even when specific identification of the thyroid and an equalized area of nearby neck background is made possible

Received Nov. 22, 1977; revision accepted Feb. 7, 1978.

For reprints contact: Marguerite T. Hays, Medical Research Service (151), Veterans Administration Central Office, 810 Vermont Ave., N.W., Washington, D.C. 20420.

by scanning (10,11) or scintillation-camera (6) techniques, inaccuracies due to inclusion or exclusion of a major blood pool or nearby salivary glands can invalidate the results.

The goal of this study was to refine the study of the thyroidal pertechnetate uptake in man by incorporating all of the information available from continuous external monitoring, correcting (insofar as possible) for the problems listed above. We aimed to simplify the complex uptake function by reducing it to a few constant descriptors, and thus to enhance its usefulness in experimental and clinical studies of the thyroidal trap. We have been using  $^{99m}\text{TcO}_4^-$  to study the human thyroidal trap, and have been examining these problems. General neck background has been handled by instrumentation, using the multicrystal camera to record our data. We have used a mathematical model for data analysis, and with it have attempted to correct neck background for vascular variability. With the model, it would be possible to detect any "very slowly reversible" pertechnetate pool in the thyroid that could become quantitatively important in the time frame of these studies. Data analysis with this model yields the specific kinetic characteristics of the pertechnetate trap. Unexpectedly, we have identified a rapidly reversible thyroidal pool, indistinguishable kinetically in our studies from intrathyroidal plasma pertechnetate, but suppressed by iodide. We postulate that this pool represents activity in the thyroid follicular cell.

#### METHODS

Subjects were paid volunteer college students, at least 21 years old. Three were men and three were women. All were euthyroid as assessed by history, physical examination, and serum concentration of thyroxine and triiodothyronine. All gave written informed consent before initiation of the studies.

Each subject underwent six experimental sessions, identical except for NaI and  $\text{KClO}_4$  medication. These studies were timed as shown in Table 1. One subject experienced tachycardia and a sense of weakness immediately after the first dose of iodide. Because of the possibility of iodine reaction, perchlorate was substituted for iodide in her fifth session, and her final session was omitted.

In this paper, we will discuss the application of the data from this experiment to model development, particularly with regard to the impact of competitive inhibition of the trap both before and during a session. Other aspects of this series of studies, including the salivary and urinary measurements and the longer-term effects of iodide on the thyroid trap, as seen in the fourth and sixth sessions, will be discussed elsewhere.

**TABLE 1. EXPERIMENTAL PLAN FOR EFFECTS OF COMPETITIVE INHIBITION OF TRAP ON MODEL**

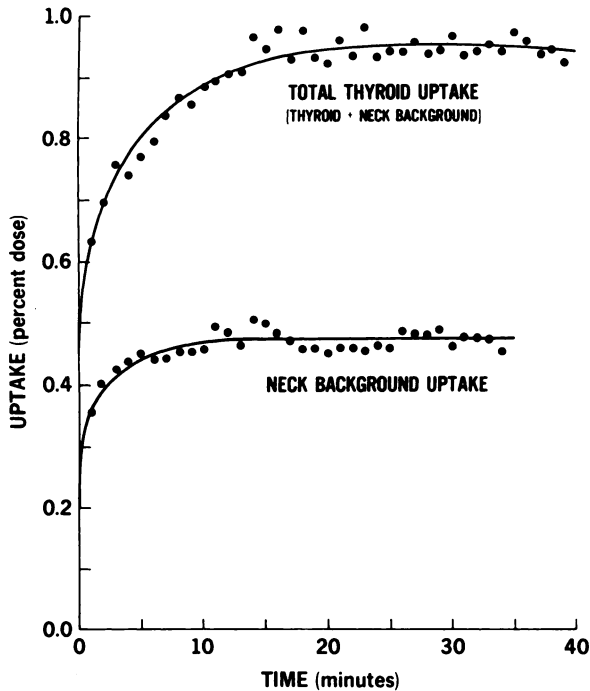
Session No.	Day No.	Experimental conditions
1	1	Control
2	3	Control
3	8	NaI 1000 mg p.o. at 20-min point in pertechnetate study
4	15	Control (postiodine)
5	22	NaI 1 g p.o. 1 hr before beginning pertechnetate study
6	29	$\text{KClO}_4$ 1 g p.o. at 20-min point in study

**Setup for each experimental session.** A uniform procedure was used for the pertechnetate study. The subject reclined on an examination table with neck extended. A plastic tube was held in the mouth, and the subject was instructed to expectorate all saliva. Saliva was collected directly in a graduated cylinder, which was changed at the 20-min midpoint of the study. An indwelling needle was placed in an antecubital vein to expedite plasma sampling, which was performed at 2, 5, 10, 20, 30, and 40 min after the pertechnetate administration. A dose of approximately 2 mCi  $^{99m}\text{TcO}_4^-$  was injected into an opposite antecubital vein at time zero. The study was terminated after 40 min and the subject collected a urine sample, generally at about 42 min.

**Measurements of Tc-99m radioactivity in the neck.** These were made with a digital multicrystal camera, an instrument that separately identifies counts in each square cm of an 11- by 19-cm array. A pinhole collimator was positioned to produce a twofold magnification of thyroid area on the detector. The standard for the neck counts was 1% of the dose, contained in a thyroid-shaped cavity in a lucite neck phantom, placed in the same position with respect to the multicrystal camera as the estimated position of the subject's thyroid gland.

Counts were collected continuously, but were summed and dumped on magnetic tape at 1-min intervals. Neck counts were initiated at the time of injection of  $^{99m}\text{TcO}_4^-$  and terminated after 40 min. The standard was counted for 10 min before and 10 min after the subject's counting period. The times of all counts were recorded for subsequent correction for radioactive decay. All camera data were corrected for field irregularities using a "flood field" measurement made with the pinhole collimator before initiation of the study.

**Handling of data stored on magnetic tape from the camera.** The magnetic tape containing the minute-by-minute 11 × 19 arrays of 1-cm<sup>2</sup> count accumula-



**FIG. 1.** Typical pertechnetate-uptake study (Subject UR). Dots represent data points. Solid line through Neck Background counts is multiexponential fit used in solution of model. Solid line through Total Thyroid Uptake is fit of data to model.

tions was later interpreted by computer. Thyroidal and neck-background areas were identified manually on computer-generated grey-scale interpretations of pooled data from ten consecutive 1-min count periods. The four separate sets of area identification (for the four time pools) were interpreted separately. If these varied substantially in location, motion of the subject during the experiment was suspected, and multiple locale identifications ("flags") were used. The locale of the standard and an appropriate background area were identified in the same way. Information about the locations of these areas of interest on the matrix was entered on the computer, which then corrected for radioactive decay and produced summed counts for each region of

interest. "Uptake" in the thyroid area and in the neck-background area (normalized to the size of the thyroid area) were calculated from the ratio to the standards.

**Handling of plasma.** Duplicate 1-ml plasma samples were pipetted into well-count tubes and counted, to a 1% or better statistical error, in a gamma spectrometer for comparison with a standard containing 0.01% of the dose.

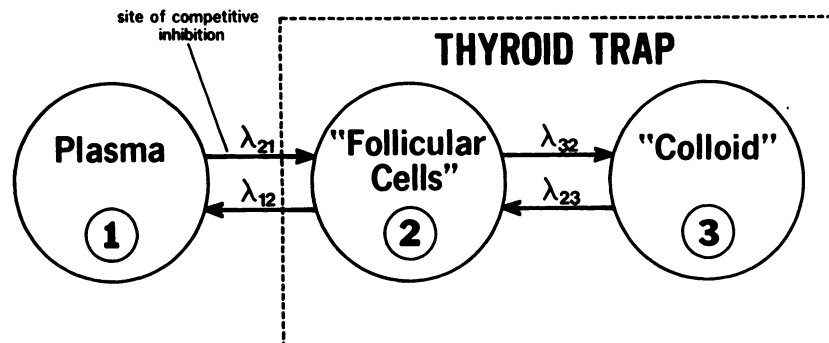
**Preliminary data analysis prior to model fit.** Individual time-point data for neck-background uptake and for plasma radioactivity were fitted to multiexponential equations for purposes of smoothing and interpolation of the data. These equations, rather than the original observed data, were used in solution of the model.

**Development and solution of the model.** These were done using the SAAM program (12) with a computer.

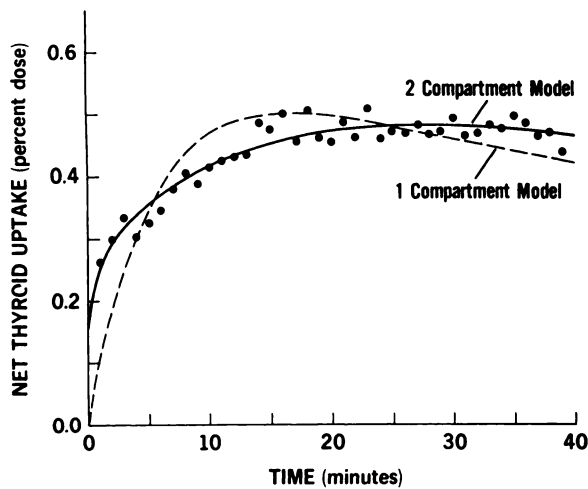
RESULTS

Typical uptake data for uncorrected thyroidal uptake and for neck background are shown as discrete points in Fig. 1. The solid lines show the result of a multiexponential fit to the neck-background data, and of a fit by the two-compartment model (incorporating the calculated neck background) to the uncorrected thyroid data. Usually the neck-background curve differed somewhat in configuration from the thyroid curve, leveling off sooner, and often decreasing at later points.

In order to utilize the known physiology of the thyroid trap in analyzing thyroidal pertechnetate kinetics, a compartmental model (Fig. 2) was developed, in which plasma pertechnetate (from the smoothing equation described above) is the input function into the trap. Because we made no attempt to measure plasma volume, the "volume" of the plasma compartment,  $V_1$ , was arbitrarily defined as 1 ml. Hence, the rate constant from plasma into the thyroid,  $\lambda_{21}$ , is equivalent to plasma clearance. Originally, the trap was represented by a single com-



**FIG. 2.** Thyroid trap model developed in this study.



**FIG. 3.** Net thyroïdal uptake curve for study shown in Fig. 1. Dashed line represents best fit with a single-compartment model. Solid line is best fit with two-compartment model.

partment,  $C_3$ , but this model was inadequate to fit the early data (Fig. 3). An additional compartment,  $C_2$ , was added representing a very rapidly exchanging compartment together with any plasma contained in the thyroïd that is not accounted for by the neck background (the "plasma differential"). Addition of this compartment improved the least-squares fit of the data, as well as improving the visual fit.

Initially, compartment  $C_2$  was thought to be just plasma, and was represented, together with neck background, as a nonthyroïdal component of the total gross thyroïd uptake. However, blocking of thyroïdal uptake by pretreatment with 1 g NaI (in Session 5) completely obliterated  $C_2$  as well as  $C_3$  in every case. In fact, in five of the six subjects,  $V_2$  was negative, suggesting a small negative "plasma differential," or overcorrection of plasma activity by neck background (Table 2). These studies were considered to show that entry into  $C_2$  is a process that is subject to competitive inhibition.

The model was then revised to place  $C_2$  in series between  $C_1$  (plasma) and  $C_3$ . Our working hypothesis is that  $C_2$  represents activity in the thyroïdal follicular cell, and that  $C_3$  represents pertechnetate contained within the follicular lumen.  $\lambda_{21}$ , the "clearance" or rate constant for the transport from plasma into  $C_2$ , is identified as the probable site of competitive inhibition.

Attempts to separate "plasma differential" from  $C_2$  by fitting of the model were unsuccessful, since the early data points were insufficient to describe the rapid equilibration phase of  $C_2$ . However, the ratio  $\lambda_{21}/\lambda_{12}$ , or  $V_2$ , the "volume" of  $C_2$ , could be clearly identified in solution of the model. Unfortu-

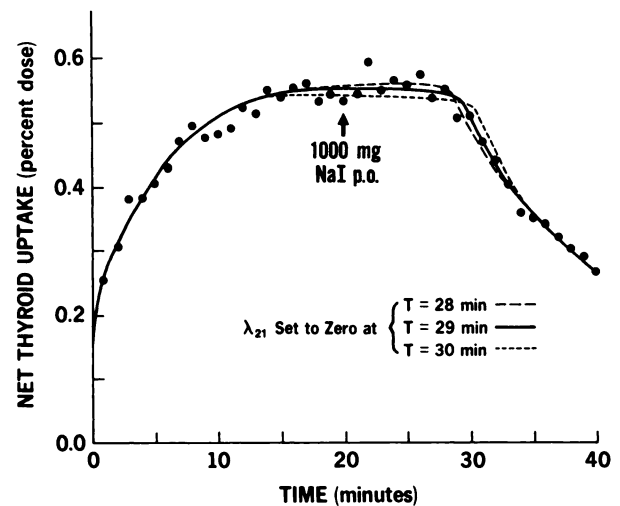
nately,  $V_2$  also contains any "plasma differential," whether positive or negative.

In its final form, the working version of the model solves for  $V_2$ , for  $\lambda_{23}$  (the exit from  $C_3$ ), and for the plasma clearance into  $C_3$ , which is the product of  $V_2$  and  $\lambda_{32}$ . In order to derive  $\lambda_{21}$  and  $\lambda_{12}$ , we assumed that a molecule, once having entered the follicular cell, has an equal chance of leaving through the apical or the basal cell membrane. By this assumption,  $\lambda_{12} = \lambda_{32}$ . It also indicates that  $\lambda_{21} = (V_2)\lambda_{32}$ .  $V_3$  is equal to  $(V_2)\lambda_{32}/\lambda_{23}$ .

When iodide or perchlorate was administered at the midpoint of the study, excellent fits were obtained by setting  $\lambda_{21}$ , the input from the plasma into  $C_2$ , to zero. No other parameters needed to be altered. Figure 4 shows such a study. The point in time when this change is made (the "change point") presumably depends upon when the blocking medication actually enters the circulation and begins to

**TABLE 2. PARAMETERS DERIVED FOR STUDIES BEGUN 1 HR AFTER BLOCKADE WITH 1 G NaI**

Subject	Sex	20-min. uptake	$V_2$ ml	$V_3$ ml
UR	F	-.03	-2.2	0.0
BO	F	.00	0.0	0.0
JO	F	-.09	-1.7	0.0
TU	M	-.01	-1.4	0.0
ST	M	.02	-2.1	0.0
FE	M	-.07	-11.6	0.0
Mean:		-.03	-3.2	0.0
SD		.04	4.2	0.0



**FIG. 4.** Net thyroïdal uptake curve for Subject UR during session in which 1 g NaI was given orally at 20 min. Model fits are shown, setting  $\lambda_{21}$  to zero at 28, 29, and 30 min.

**TABLE 3. "CHANGE POINTS": EXPERIMENTAL TIME WHEN  $\lambda_{21}$  BECAME ZERO AFTER ADMINISTRATION OF 1 G OF NaI OR 1 G KClO<sub>4</sub> AT 20 MIN**

Subject	Oral KClO <sub>4</sub>	Oral NaI	i.v. NaI
UR	21	29	
BO		36*	
JO	26	29	20
TU	23	24	
ST	22	25	
FE	27	36	

\* Questionable iodine reaction (see text).

reach the thyroid gland. This "change point" is quite well defined by the model. In Fig. 4, three fits are shown, differing only in that the "change point" differed by 1 min. The middle curve appears to fit the portion of the data near the "change point" best. Table 3 lists the individual subjects' "change points" after administration of iodide and perchlorate. While the differences are not great, the subjects found NaI to be less palatable than the KClO<sub>4</sub>, and gastric emptying could well have been slower after the NaI. Subject JO later had an additional study in which NaI was given at 20 min intravenously instead of orally. In that study, the "change point" occurred

at 20 min, as expected. In the session in which the questionable iodine reaction (described above) occurred, and also one other iodide study, gastric emptying appears to have been delayed.

Table 4 presents the calculated parameters for the control studies of Sessions 1, 2, and 3. The 20-min thyroidal uptake is shown for comparison. Session 1 studies of two subjects were lost due to instrumental difficulties, so completed double-control studies are available for only four subjects. Subject JO had a repeat control study 1 yr later, before the i.v. NaI study.

DISCUSSION

The technique used for collection of these data, using the multicrystal camera and subsequent computer analysis of regions of interest, appears to yield results qualitatively and quantitatively comparable with results we now get using a scintillation camera with computer analysis of the regions of interest. Similarly, our results are qualitatively compatible with studies done in England and Scotland in 1967 and 1968 using sequential rectilinear scanning techniques (10,11). The gross 20-min uptakes in our subjects, however, are considerably smaller than those reported in either of those series. We believe that this reduced pertechnetate "uptake," with a correspondingly lower thyroidal plasma clearance, is a

**TABLE 4. PARAMETERS CALCULATED BY FITTING DATA TO TWO-COMPARTMENT MODEL.**

Subject	Session	20-min uptake	V <sub>2</sub> ml	V <sub>3</sub> ml	(Clearance)			Comment
					$\lambda_{21}$ ml/min	$\lambda_{21}/$ min	$\lambda_{12} = \lambda_{32}/$ ml	
UR	1	.59	41	63	3.5	.055	.09	
	2	.47	20	54	3.3	.062	.17	
	3*	.51	17	59	5.3	.089	.31	NaI at 20 min
BO	1	.36	3	57	2.4	.042	.80	
	2	.38	10	41	2.5	.060	.25	
	3*	.28	12	38	1.5	.038	.13	NaI at 20 min
JO	2	.77	12	193	5.3	.028	.44	
	3*	.49	11	95	3.4	.038	.31	NaI at 20 min
	7	.53	11	70	3.0	.043	.27	1 year later
TU	1	.43	5	59	6.0	.102	1.20	
	2	.68	23	89	9.1	.103	.40	
	3*	.58	39	149	2.9	.020	.07	NaI at 20 min
ST	1	1.06	24	378	5.6	.015	.23	
	2	1.09	22	324	5.7	.018	.26	
	3*	1.34	22	452	11.0	.024	.50	NaI at 20 min
FE	2	.82	17	236	6.3	.027	.37	
	3*	.57	15	141	4.3	.031	.29	NaI at 20 min
Parameters for mean model:		.64	18	102†	4.8	.047	.27†	
SD		.29	10		2.5	.028		

\* In Session 3 (1 G NaI given at 20 min),  $\lambda_{21}$  was set to zero at the "change point," with all other parameters unchanged.

† As these parameters are secondary, calculated from the other (primary) parameters, the values presented as means are derived from the means of the primary parameters rather than from the means of individual calculated parameters. The latter are 147 for V<sub>2</sub> and .36 for  $\lambda_{12}$  and  $\lambda_{32}$ .

function of increased dietary iodine with both time and locale.

The model described in this paper was based upon the known physiology of the thyroidal iodide-concentrating mechanism, understanding of which has changed little since the comprehensive review by Wolff in 1964 (13). It is consistent with the general pertechnetate distribution model of Hays and Berman (14), but incorporates only the plasma and thyroid compartments of that model, with subdivision of the thyroid compartment. Structure of our model is similar to that of the models proposed by Wollman and Reed (15). Initially, we considered the intrathyroidal ion to represent a single compartment ( $C_3$ ), comparable to Wollman and Reed's "two-compartment open model." However, fitting of the early data (Fig. 3) required that a second, faster, thyroidal compartment ( $C_2$ ) be added. Initially we considered this to represent intrathyroidal blood pool not corrected by neck background, since we could not clearly distinguish it kinetically from plasma. The volumes calculated for this compartment, however, were greater than those expected for an uncorrected blood pool. Our doubts about a blood-pool identity for this compartment were confirmed when we found that iodide block inhibited  $C_2$  as well as  $C_3$ .

While we have no direct evidence about the anatomic or physiologic nature of  $C_2$ , review of the work of Andros and Wollman (16) suggests that it represents concentration of the pertechnetate ion in the follicular cell. By radioautographic techniques in the propylthiouracil-blocked mouse thyroid, these workers demonstrated that there is a transient phase, 2–10 min after radioiodide injection, when the radioiodide concentration in the follicular cell is greater than the concentration seen in the lumen of the follicle.

Solution of the model does not require that  $C_2$  and  $C_3$  be in series. This configuration was chosen because it appears logical. It is compatible with the Wollman-Reed open three-compartment model, or alternatively, with a carrier model, as suggested by Lewellen and reported by Wolff (13).

We were not able to achieve unique solutions for  $\lambda_{21}$  and  $\lambda_{12}$ , presumably because the quality of our early experimental data is insufficient to separate  $C_2$  temporally from plasma.  $V_2$ , the plasma equivalent of  $C_2$ , however, is uniquely soluble. In order to calculate  $\lambda_{12}$  and  $\lambda_{21}$ , we have assumed that, after equilibration, the flux (in plasma-equivalent volume) of pertechnetate is the same from plasma to  $C_2$ , and from  $C_2$  to  $C_3$ . This assumption will hold if there is an equal likelihood that a pertechnetate ion, once having entered the follicular cell, will exit through

the basal or the apical cell membrane. We are aware of no evidence to confirm or to refute this hypothesis.

The model solves for  $[V_2 \times \lambda_{32}]$ , the plasma-equivalent clearance into compartment 3, and for  $\lambda_{23}$ , the exit constant from compartment 3.  $V_3$ , the plasma-equivalent volume of compartment 3, is derived from the ratio of these parameters. Although unique solutions for  $[V_2 \times \lambda_{32}]$  and for  $\lambda_{23}$  were generally achieved with no difficulty, in a few cases these could be altered within a narrow range without impairing fit. When this occurred, we observed that, if either  $[V_2 \times \lambda_{32}]$  or  $\lambda_{23}$  was altered arbitrarily while the other was adjusted by the program to fit the data best, the ratio of  $[V_2 \times \lambda_{32}]$  to  $\lambda_{23}$  (i.e.,  $V_3$ ) tended to remain constant.

After competitive inhibition of  $\lambda_{21}$  by a massive dose of iodide or perchlorate during the course of a study, the only alteration in the model that had to be made to achieve good fit was to reset  $\lambda_{21}$  to zero. This change was both necessary and sufficient to account for the iodide effect. There was no need for an additional, irreversible compartment. The same exit constants fitted the curve both before and after inhibition of  $\lambda_{21}$ . This finding does not conflict with the work of Burke et al. (6), since the irreversible compartment that they showed was found in hyperthyroid but not in normal subjects.

This model is being applied to analysis of data from a variety of clinical and experimental situations. Results of these studies will be reported elsewhere.

#### ACKNOWLEDGMENTS

The author thanks Mones Berman for his patient instruction in modeling techniques, for his generous advice during the progress of this work, and for making the facilities of his laboratory available. Dr. Berman's associates in the Laboratory of Theoretical Biology of the National Cancer Institute were uniformly generous in their advice and assistance.

Ms. Jordana Witheiler and Ms. Sara Paul provided excellent technical assistance.

#### REFERENCES

1. ANDROS G, HARPER PV, LATHROP KA, et al: Pertechnetate-99m localization in man with applications to thyroid scanning and the study of thyroid physiology. *J Clin Endocrinol Metab* 25: 1067–1077, 1965
2. SOCOLOW EL, INGBAR SH: Metabolism of <sup>99m</sup>Pertechnetate by the thyroid gland of the rat. *Endocrinology* 80: 337–344, 1967
3. PAPAPOPOULOS S, MACFARLANE S, HARDEN R MCG: A comparison between the handling of iodine and technetium by the thyroid gland of the rat. *J Endocr* 38: 381–387, 1967
4. SHIMMINS JG, HARDEN R MCG, ALEXANDER WD: Loss

- of pertechnetate from the human thyroid. *J Nucl Med* 10: 637-640, 1969
5. HECK L, LATHROP K, GOTTSCHALK A, et al: Perchlorate washout of pertechnetate from the thyroid gland. *J Nucl Med* 9: 323, 1968 (Abst)
6. BURKE G, HALKO A, SILVERSTEIN GE, et al: Comparative thyroid uptake studies with  $^{131}\text{I}$  and  $^{99\text{m}}\text{TcO}_4^-$ . *J Clin Endocr* 34: 630-637, 1972
7. WOLFF J, MAUREY JR: Thyroidal iodide transport IV. The role of ion size. *Biochim Biophys Acta* 69: 58-67, 1963
8. HAYS MT, GREEN FA: In vitro studies of  $^{99\text{m}}\text{Tc}$ -pertechnetate binding by human serum and tissues. *J Nucl Med* 14: 149-158, 1973
9. HAYS MT, WESSELOSSKY B: Simultaneous measurement of thyroidal trapping ( $^{99\text{m}}\text{TcO}_4^-$ ) and binding ( $^{131}\text{I}$ ): Clinical and experimental studies in man. *J Nucl Med* 14: 785-792, 1973
10. SHIMMINS J, HILDITCH T, HARDEN R MCG, et al: Thyroidal uptake and turnover of the pertechnetate ion in normal and hyperthyroid subjects. *J Clin Endocrinol Metab* 28: 575-581, 1968
11. DE GARRETA AC, FISICAS CS, GLASS HI, et al: Measurement of the uptake of  $^{99\text{m}}\text{Tc}$  by the thyroid. *Br J Radiol* 41: 896-898, 1968
12. BERMAN M, SHAHN E, WEISS MF: The routine fitting of kinetic data to models: a mathematical formalism for digital computers. *Biophys J* 2: 275-288, 1962
13. WOLFF J: Transport of iodide and other anions in the thyroid gland. *Physiol Rev* 44: 45-90, 1964
14. HAYS MT, BERMAN M: Pertechnetate distribution in man after intravenous infusion: A compartmental model. *J Nucl Med* 18: 898-904, 1977
15. WOLLMAN SH, REED FE: Transport of radioiodide between thyroid gland and blood in mice and rats. *Am J Physiol* 196: 113-120, 1959
16. ANDROS G, WOLLMAN SH: Autoradiographic localization of radioiodide in the thyroid gland of the mouse. *Am J Physiol* 213: 198-208, 1967

### WORLD FEDERATION OF NUCLEAR MEDICINE AND BIOLOGY

The Second International Congress of the World Federation of Nuclear Medicine and Biology will be held Sept. 18-21, 1978, at the Washington Hilton Hotel, Washington, D.C.

The program will consist of scientific and public symposia, including 300 papers on basic sciences and clinical applications of radioactive tracers, CT and ultrasound, teaching sessions, and exhibitions.

For further information, including submission of abstracts, please write:

**Henry N. Wagner, Jr., General Chairman**  
**WFNMB Second International Congress**  
**1629 K Street, NW, Suite 700**  
**Washington, DC 20006**

For further information regarding exhibits, please write:

**Exhibit Headquarters, WFNMB**  
**Society of Nuclear Medicine**  
**475 Park Avenue South**  
**New York, NY 10016**