Neutron-Activation Measurement of Metabolic Activity of Sodium in the Human Hand

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Turnover of sodium in the human hand was studied by neutron activation. One hand of each subject was irradiated with a 1.5-rad dose of partially thermalized fast neutrons. The activity of ^{24}Na was measured at intervals from 3 min to 48 hr after irradiation. The loss of sodium from the hand during this period can be described either by two exponentials or by a single power function. The latter description involves only two disposable factors compared with four in the former. The rate of loss of sodium was found, on the average, to be greater in patients suffering from bone disease than in normal subjects. Neutron activation is a powerful method for studying sodium turnover because the sodium atoms are labeled simultaneously and with equal probability, regardless of the turnover time of individual bodily compartments.

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Neutron activation is normally used in the life sciences to measure the quantities of certain elements present in an organism (living or dead), in a part of the organism, or in a biopsy specimen. Here we will be concerned instead with the study of dynamic processes. As far as we are aware, the only comparable application of neutron activation (*1*) used cold neutrons from a reactor to study the loss of Na, Cl, and Ca from a superficial area of the human tibia. We have studied the dynamics of sodium in the human hand after irradiation by partially thermalized fast neutrons.

Ethical considerations require that no subject receive unnecessary irradiation. The subjects in the present study were a number of patients suffering from bone diseases who received neutron irradiation to one hand in order to measure its calcium content as an aid in evaluating prior treatment. We used the opportunity to measure the metabolic activity of sodium as well. In addition, a few normal volunteers received irradiation to the hand. These were members of the staff and the doses delivered were kept well below the maximum permissible levels for occupationally exposed persons.

At such low levels of irradiation only the major body elements can be measured, and of these only sodium (as ^{24}Na) has a long enough half-life (15 hr) to permit metabolic processes to be followed for more than an hour or so. Much of the body sodium is in bone, where turnover is so slow that the usual isotope-dilution technique is unworkable (*2,3*). In contrast, neutrons activate the sodium atoms simultaneously and with equal probability, regardless of whether they are in bone or soft tissue.

METHODS

Sodium-24 is formed by the thermal-neutron capture reaction ^{23}Na(n,γ)^{24}Na. The fast-neutron beam from the MRC cyclotron, of mean energy 7.5 MeV, was used for irradiation (*4*). The fluence of thermal

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neutrons was increased by means of a "moderator" of paraffin wax surrounding the hand. The arrangement is shown in Fig. 1. The subject's left hand was placed in the moderator, the front of which was at the normal position for neutron therapy, namely, 120 cm from the target (*4*). The average thickness of wax was 6 cm. The field size was 21 × 21 cm incident on the moderator, and the average irradiation time was 30 sec. During irradiation the fingers were held straight with the tips touching the end of the cavity. The right hand was shielded from the neutrons by placing it in a cadmium-lined wax cylinder.

Within 2–3 min after irradiation, the subject was transferred to a whole-body counter containing four NaI(Tl) detectors, each 15 cm in diameter and 10 cm thick. These were arranged in two opposed pairs, with the surfaces of the crystals separated by 8 cm and the centers of the two pairs about 40 cm apart. Each hand was placed prone between one pair of detectors, the positions of the hands being defined by Perspex frames.

During irradiation of the left hand, all parts of the body except the right hand became slightly active due to stray neutrons. Apart from the natural background, therefore, the count rate in the detectors monitoring the unirradiated hand was due to (A) residual activity in parts of the body other than the hands; (B) activity transferred from other parts of the body to the control hand; and (C) blood-borne activity from the irradiated hand to the rest of the body. Hence, measuring the activities of the shielded right hand and the activated left hand simultaneously provided a measure of all background effects.

The efficiency of the sodium measurement is proportional to the product of the efficiencies of activation and counting. The efficiency of activation was determined by measuring the activity induced in gold foils taped along the back and front of the hand of one subject, and the efficiency of counting was determined by measuring the variation of count rate due to a ^{228}Th point source of 2.62-MeV photons placed at different positions in the Perspex frame. In this way the total efficiency was found to be a maximum at the position of the knuckles and fell to one-third at the tip of the second finger and to about 5% at the wrist.

Figure 2 shows spectra measured over 20 min beginning at 2.5 and 64 min after activation. Of the two lines from ^{24}Na, that at 2.75 MeV was used. Interference at this energy arises from 8.9-min ^{49}Ca, plus a small contribution from 5.1-min ^{37}S formed in low yield by the ^{37}Cl(n,p)^{37}S reaction. Both these nuclides emit photons at 3.1 MeV. The 1.37-MeV line of ^{24}Na has the disadvantages that the natural background is much higher there than at 2.75 MeV and that there is additional interference from ^{28}Al and ^{38}Cl. Aluminum-28 is formed by the fast-neutron reaction ^{31}P(n,α)^{28}Al and emits 1.78-MeV photons, while ^{38}Cl is formed from thermal-neutron capture by ^{37}Cl and emits photons at 1.60 and 2.17 MeV. Counts from ^{24}Na were integrated over the range 2.59–2.97 MeV, and the contribution from ^{49}Ca and ^{37}S was subtracted, where necessary, on the basis of the spectrum obtained by activating a model hand containing Ca(NO$_3$)$_2$. From phantom studies we estimate that the sodium from the ^{24}Mg(n,p)^{24}Na reaction is less than 2% of the total ^{24}Na formed.

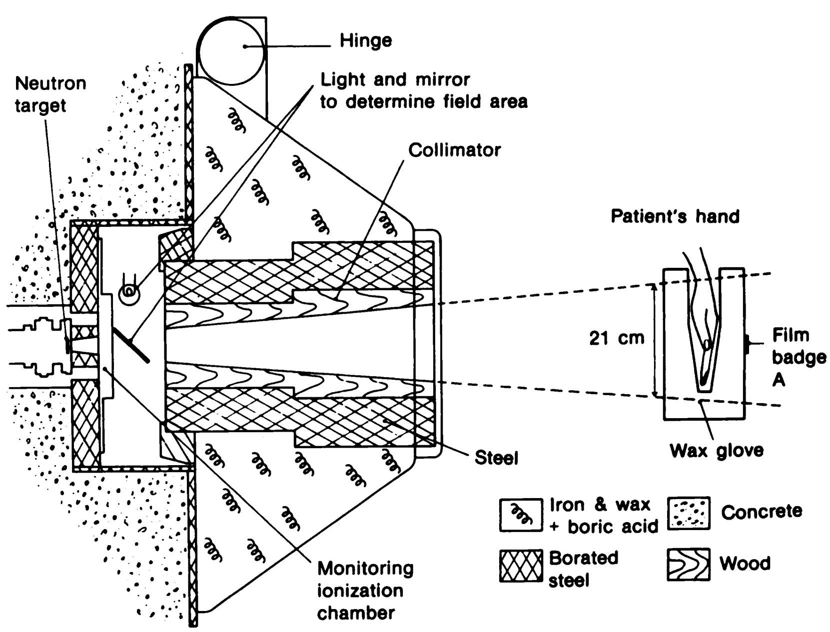

FIG. 1. Plan view of arrangement for irradiating hand.

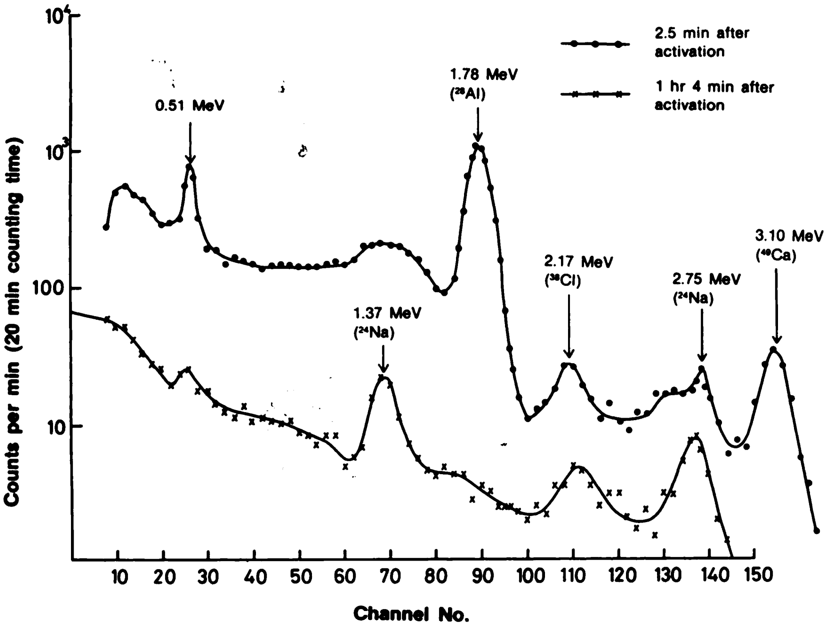

FIG. 2. Two gamma spectra of activated hand measured for 20 min, starting at 2.5 min and at 64 min after irradiation.

Dosimetry. The dose of neutrons was controlled by an air-filled monitoring chamber. This chamber is regularly calibrated for neutron therapy to indicate the neutron dose at 120 cm from the target (*4*). The neutron and gamma-photon doses at the hand were derived from this calibration by experiments with a pair of ionization chambers having walls of polythene and aluminum (*5*). In addition, the dose-equivalent at the hand was estimated from a fast-neutron film badge supplied by the National Radiological Protection Board and placed on the back of the wax moderator (position A of Fig. 1). The neutron dose to the hand at the corresponding position was measured with the pair of ionization chambers, and the film badge reading was adjusted accordingly. Table 1 gives the dose and dose-equivalent for the left hand of each subject.

The average dose-equivalent to the whole body was estimated by distributing films over the body of a volunteer who stood in the normal position but with his hand not in the wax moderator and by measuring the quantity of ^{24}Na produced in the body of this volunteer. The films indicated values varying from 0.03 to 0.12 rem, while the amount of ^{24}Na was the same as that produced in a patient receiving 0.14 rem to the whole body during total-body activation analysis. Thus, the average dose-equivalent to the body was about 0.1 rem and below 0.2 rem. Occupationally exposed workers must not receive more than 37 rem per quarter or 75 rem per year to the extremities, or 3 rem per quarter to the whole body (*6*). Our procedure involves considerably less radiation than this and is not repeated on the same person more than once or twice in the same year.

RESULTS

Two-component analysis. Figure 3 illustrates, for patient No. 7, the decay-corrected count rate from ^{24}Na (on a semilogarithmic scale) as a function of time. The time t is taken from the end of irradiation to the middle of the counting period. Although errors for the later counts are considerable, the data can be fitted by a sum of two exponentials of the form

$$C(t) = A_1 e^{-\lambda_1 t} + A_2 e^{-\lambda_2 t}, \qquad (1)$$

TABLE 1. DOSES RECEIVED BY THE HAND

	Dose measured by ion chamber (rad)		Dose-equivalent measured by film badge (rem)
	neutrons	gamma photons	
Patients			
1	1.5	0.2	16
2*	1.5	0.2	16
	1.6	0.2	17
3	1.5	0.2	16
4	1.5	0.2	—
5	1.6	0.2	—
6	1.6	0.2	—
7	1.6	0.2	17
8	1.6	0.2	15
Normal subjects			
9*	1.1	0.1	9
	1.5	0.2	14
10	1.3	0.2	—
11	1.5	0.2	—
12	1.6	0.2	15

* Patient No. 2 and normal subject No. 9 were studied twice.

where C is the count rate and A_1, A_2, λ_1, and λ_2 are positive constants. If there are more than two clearance compartments, they cannot be resolved from the data with any certainty. This two-component analysis also fits the data from all but one of the other subjects (Patient No. 4 gave anomalous results with large errors). The values determined for the constants are given in Table 2. Ignoring the data from Patient No. 4, the range of half-times for the faster clearance is 26 ± 5 min to 208 ± 36 min and that for the slower clearance is 28 ± 15 hr to infinity, the latter implying, of course, a completely nonexchangeable compartment. The component with the faster clearance accounts for 60–80% of the total activity 3 min after irradiation.

Power law model. For comparison, the data of Fig. 3 are plotted on a double-logarithmic scale in Fig. 4. This treatment indicates that the loss of radiosodium from the hand can also be described, to a close approximation, by a power law of the form

$$C = Bt^{-x}, \qquad (2)$$

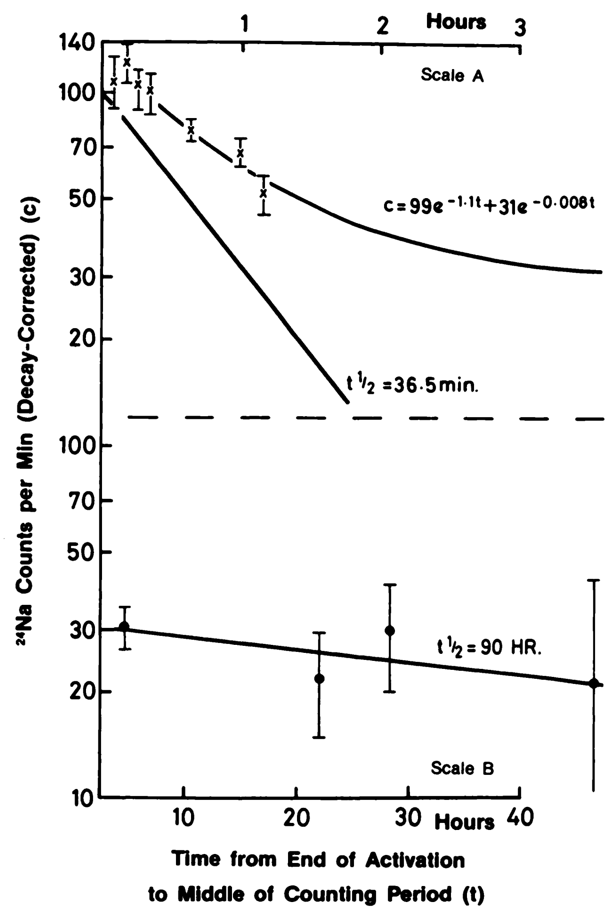

FIG. 3. Log activity of ^{24}Na as function of time after irradiation in patient No. 7. Scale A shows fast component ($t_{1/2}$ = 36.5 min), along with fitted curve, and scale B shows slow component ($t_{1/2}$ = 90 hr).

where B depends on the amount of sodium in the hand and the dose received, and x is a measure of the rate of washout. Similarly, the data for all other experiments closely follow a similar power law. The apparent tendency of the curve to flatten off at about t = 0.1 hr suggests that a better fit might be obtained by use of the equation

$$C = B(t + \tau)^{-x}, \qquad (3)$$

where τ is another positive constant. This equation makes more physical sense than Eq. 2 because C remains finite when t = 0. However, Eq. 2 provides a good fit over the time period considered, and we have not attempted to use Eq. 3 in the analysis of our results. Values for the constants B and x, obtained by a weighted least-squares fit, are given in Table 2. With the exception of patients No. 2 (first measurement) and No. 8, the rate of exchange of sodium is greater in the patients than in the normal subjects (i.e., the value of x is larger).

DISCUSSION

The semilogarithmic plot of Fig. 3 is similar to that found by Comar et al. (*1*) for the tibia. They found a half-time of 35 min for sodium in one subject, which is close to our finding. Their value for the quickly exchangeable fraction, however, was only 44% compared with our values of $A_1/(A_1 + A_2)$, which ranged over 60–83%. The different proportions of quickly exchangeable sodium may be due to the different regions of the body studied or to the fact that we were able to give the irradiation in a shorter time and to begin counting with less delay. Comar's group identified the two components with sodium in bone and soft tissue, but the excellent fit to a power law (Fig. 4) found for every subject in our study suggests that analysis in terms of only two compartments is an oversimplification.

Studies with injected isotopes of calcium have shown that the decrease of serum specific activity with time is often fitted better by a power law than by a combination of exponentials (*7,8*). An equation of the form

$$C = At^{-\alpha}e^{-\beta t} \qquad (4)$$

has also been proposed (*9*). In this expression, the constant β is small, and deviation from a power function does not normally occur until 10–50 hr after injection. The situation in those experiments, however, was complicated by the tracer's having to pass into the various body compartments before it could begin to move out again. Compartments that turn over slowly (bone) would still be filling while those with quicker turnover were emptying. Indeed, Burkinshaw et al. (*10*) proposed a model of bone turn-

TABLE 2. VALUES OF THE CONSTANTS IN EQUATIONS 1 AND 2 (mean ± s.e.m.)

Patient data				Two-exponential model				Power-law model		X-ray findings in hand and arm
No.	Age	Sex	Diagnosis	A_1 (cpm)	A_2 (cpm)	λ_1 (hr^{-1})	λ_2 (hr^{-1})	B (cpm)	x	
1	64	M	Paget's disease	110 ± 3	51 ± 1	1.2 ± 0.1	0.011 ± 0.002	81	0.30 ± 0.04	Degenerative changes
2	51	F	Osteoporosis	69 ± 2	32 ± 2	0.56 ± 0.05	0.000 ± 0.003	63	0.25 ± 0.03	Minor degenerative changes
	53	F	Osteoporosis	91 ± 34	34 ± 15	1.2 ± 0.2	0.011 ± 0.006	64	0.31 ± 0.02	Minor degenerative changes
3	58	F	Paget's disease	83 ± 7	31 ± 5	0.67 ± 0.06	0.017 ± 0.006	61	0.35 ± 0.02	Normal
4	62	F	Paget's disease	185 ± 200	86 ± 7	7.3 ± 6.3	0.14 ± 0.03	73	0.34 ± 0.05	Pagetic involvement of distal radius
5	47	F	Hyperparathyroidism	*	*	0.91 ± 0.17	0.013 ± 0.010	55	0.36 ± 0.03	No abnormalities
6	63	F	Osteoporosis	89 ± 21	39 ± 19	0.89 ± 0.16	0.023 ± 0.009	69	0.34 ± 0.04	Degenerative changes in interphalangeal joints
7	74	F	Osteoporosis	99 ± 6	31 ± 3	1.1 ± 0.1	0.008 ± 0.006	64	0.33 ± 0.03	General osteoporosis
8	72	M	Osteoporosis	126 ± 21	26 ± 20	0.20 ± 0.03	0.00 ± 0.01	114	0.24 ± 0.03	General osteoporosis
9	26	M	Normal	54 ± 14	27 ± 10	0.6 ± 0.1	0.004 ± 0.009	49	0.27 ± 0.03	
	26	M	Normal	89 ± 38	51 ± 43	1.6 ± 0.3	0.025 ± 0.013	71	0.28 ± 0.02	
10	32	M	Normal	81 ± 13	55 ± 10	0.78 ± 0.11	0.012 ± 0.003	89	0.25 ± 0.02	
11	51	M	Normal	95 ± 11	41 ± 6	1.2 ± 0.1	0.005 ± 0.002	75	0.27 ± 0.03	
12	45	F	Normal	89 ± 11	38 ± 12	0.35 ± 0.08	0.001 ± 0.001	92	0.24 ± 0.02	

* Insufficient data to calculate A_1 and A_2.

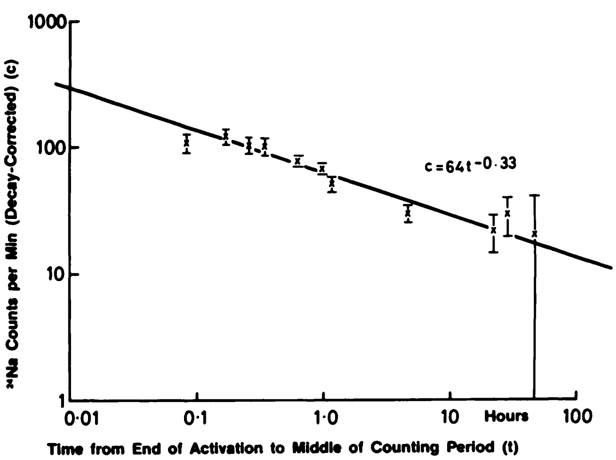

FIG. 4. Log activity of ^{24}Na as function of log time after irradiation for patient No. 7.

over based on a continuously expanding exchangeable calcium pool; they arrived at an expression for serum specific activity not very different from Eq. 4.

The total quantities of sodium and calcium in the hand at the time of the first count were estimated by comparison with irradiated hand-shaped phantoms containing solutions of sodium and calcium nitrate. The sodium in bone was then found by multiplying the calcium content by the sodium-to-calcium ratio in bone (3.38 wt%) given by the ICRP (*11*). This approach indicates that about half the total sodium in the hand at the time of the first count was in the bone. This can be compared with the results of chemical analysis of cadavers, which indicate that about 40% of the total-body sodium is in bone (*12*). One would expect a larger proportion from our experiments, because any ^{24}Na produced in the vascular system would be washed out during the 3-min interval before counting began and because the hand contains a higher proportion of bone than the whole body. These proportions of hand sodium in bone are larger than those indicated by the two-exponential analysis [$A_2/(A_1 + A_2) = 17$–40%], reinforcing the point made above that these two components should not be closely identified with bone and soft tissue.

The power-law model involves only two disposable constants (B and x) compared with four (A_1, A_2, λ_1, and λ_2) for the two-exponential model, and these two constants can be determined with greater precision. A distinction between patients and normal subjects does not emerge from the analysis by two exponentials. The dependence of the quantity x on the state of bone disease suggests that it is a measure of the metabolic activity of the bone. Furthermore, Burkinshaw et al. (*10*) found that the loss of ^{47}Ca from plasma to bone closely fitted a power law for the first 24 hr, with the exponent x varying from 0.17 to 0.42 with a mean of 0.28. The similarity between the kinetics of sodium loss from the hand and that of calcium deposition in the skeleton provides strong evidence that the two processes are closely linked.

Studies with animals would be needed for a less ambiguous understanding of the quantities and exchange rates of sodium in different tissues of the body. The method reported here, however, using activation analysis, throws fresh light on the turnover of sodium in the human hand because it avoids the problem of slow exchange in some body compartments, which complicates the interpretation of results obtained by the isotope-dilution method.

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