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MAJOR SOURCES OF ERROR IN INTERPRETING URINALYSIS DATA TO ESTIMATE THE BODY BURDEN OF Pu^{239}: A PRELIMINARY STUDY

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Abstract—Several methods of estimating the body burden of Pu^{239} from urinalysis data have been reported, and two of these have been coded for a digital computer. Intercomparison indicates that uncertainty by a factor of two or more may be present in some of these methods. The code PUQUAE has been tested, using data on hospital patients following a single intravenous injection of Pu^{239}. When a continuous rate of excretion curve is determined for each patient, the code estimates the intake to within some 30 per cent. It is concluded that individual variation, spacing of intake between sample dates, and the use of a true rate of excretion curve as opposed to a formula predicting discrete daily excretions are major sources of uncertainty in this method. While the data obtained are suggestive, the number of cases and hypotheses tested is small, and a firm estimate must be based on more extensive data.

LAWRENCE[1] has described a code for the IBM 704 computer which analyzes the urinalysis data of an individual occupationally exposed to Pu^{239} and thereby produces an estimate of his body burden. This code, designated as PUQFUA, uses a power function to describe the excretion of Pu^{239} following a single intravenous injection and estimates a series of single intakes into blood that would produce the observed concentrations in urine. When the intakes estimated for times prior to a given sample date indicate a greater output of plutonium than was actually observed, one of the previously estimated intakes is rejected. In general, such rejection results from the elimination of certain sample values at earlier times.

To avoid this rejection of data, a code for the IBM 7090 computer has been written which treats intake into blood and excretion from blood as continuous functions of time, rather than as discrete quantities, and does not reject any data points.[2] It is necessary, however, to interpolate values for the urinary output between observed values. Two such codes have been reported[2]—PUQUAP, which assumes a power function model for retention as well as for excretion following a single intake, and PUQUAE, which differs only in assuming the fraction of a single intake remaining at time t is 1 minus the total excretion, the latter being also represented as a power function. Figure 1 summarizes excretion data obtained by LANGHAM[3] on terminal hospital patients, and the power functions indicated are, with minor modifications, the basis for all the methods of estimation discussed above.

Table 1[2] shows estimated body burdens of 26 employees with long-term potential exposure to Pu^{239}. The estimates of Langham are shown in the second column and are based on his personal evaluation of the individual's record. The value marked by [c] is based on autopsy data and probably deserves to be considered as the most accurate estimate in Table 1. The third column lists the estimates obtained by PUQFUA, and the fourth column shows the number of data values rejected. Columns 6 and 8 list estimates by PUQUAP and PUQUAE, respectively, when a single intake is postulated to occur 15 days

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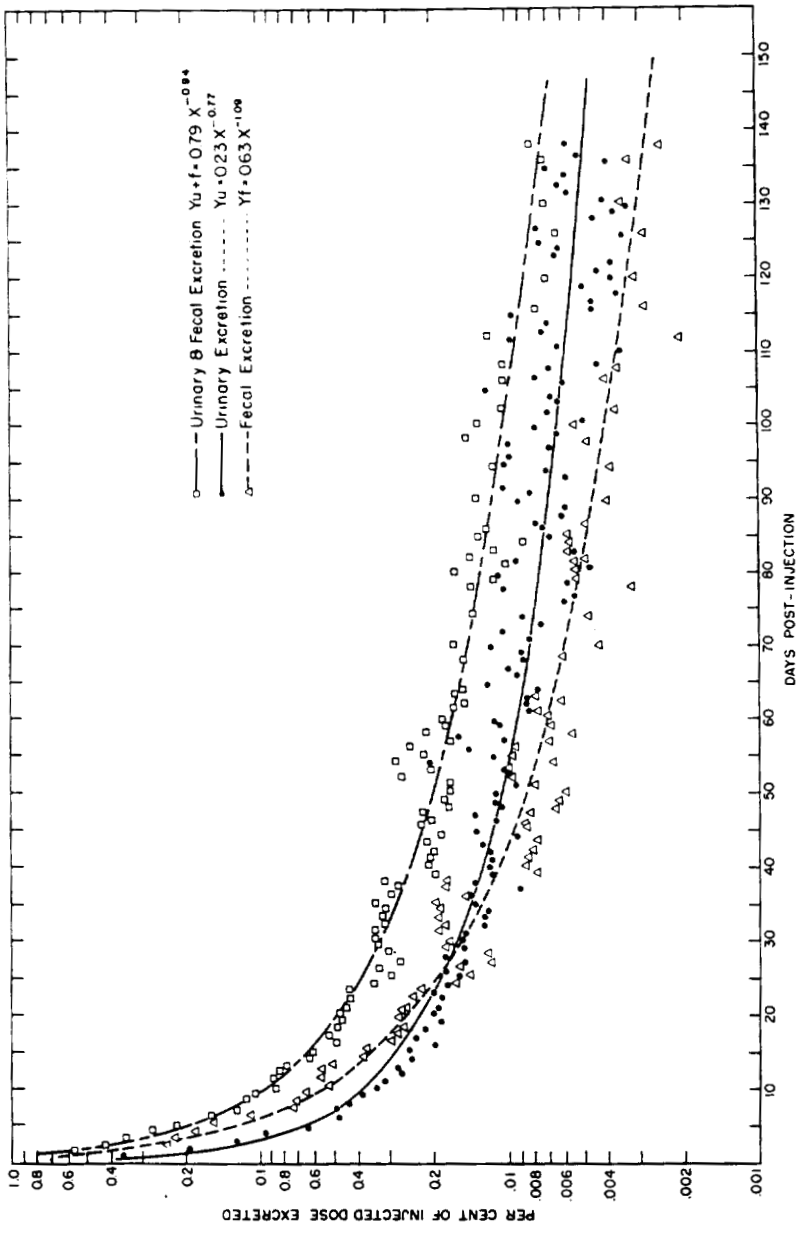

FIG. 1. Observed means for urinary, fecal and urinary and fecal excretion of plutonium following intravenous injection, compared with their derived expressions.

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Table 1. Comparison of plutonium body burden estimates

Code	LANGHAM	PUQFUA	PUQFUA invalidated samples	PUQUAP[a]	PUQUAP[b]	PUQUAE[a]	PUQUAE[b]
C135	0.08	0.1382	16	0.0882	0.1002	0.0758	0.0861
D334	0.07	0.1336	2	0.1002	0.1058	0.0872	0.0921
D711	0.07	0.1375	1	0.0901	0.1312	0.0785	0.1142
G717	0.06	0.0732	2	0.1340	0.1488	0.1168	0.1297
D63	0.06	0.1137	0	0.0702	0.0769	0.0611	0.0670
E36	0.06	0.0797	1	0.0739	0.0784	0.0644	0.0683
C397	0.05	0.0294	5	0.0454	0.0456	0.0390	0.0391
D501	0.04	0.0552	2	0.0376	0.0407	0.0328	0.0355
F664	0.04	0.0934	0	0.0511	0.0540	0.0445	0.0471
G716	0.04	0.0350	1	0.0242	0.0407	0.0211	0.0355
E742	0.03	0.0579	2	0.0490	0.0539	0.0427	0.0469
D775	0.02	0.0250	5	0.0231	0.0284	0.0201	0.0246
D182	0.02	0.0233	1	0.0179	0.0296	0.0156	0.0258
G524	0.02	0.0227	2	0.0177	0.0254	0.0154	0.0221
E629	0.02	0.0277	1	0.0165	0.0256	0.0144	0.0223
E390	0.02	0.0174	1	0.0173	0.0201	0.0151	0.0175
D791	0.02	0.0278	2	0.0205	0.0230	0.0178	0.0200
D591	0.02	0.0398	1	0.0213	0.0235	0.0186	0.0205
D205	0.02	0.0397	0	0.0156	0.0192	0.0136	0.0168
C137	0.02	0.0286	17	0.0350	0.0350	0.0300	0.0300
F634	0.01	0.0418	0	0.0478	0.0478	0.0413	0.0413
E252	0.01	0.0233	2	0.0173	0.0174	0.0150	0.0151
F412	0.006	0.0112	2	0.0103	0.0119	0.0090	0.0104
D670	0.006	0.0020	2	0.0179	0.0219	0.0156	0.0191
C365	0.006	0.0114	10	0.0090	0.0157	0.0077	0.0135
E822	0.032	0.0186	20	0.0296	0.0299	0.0255	0.0257
E822	0.0175[c]						

[a] Assumes exposure begins on date of first sample.
[b] Assumes exposure begins 15 days before date of first sample with urine count predicted by excretion formula.
[c] Body burden estimate from autopsy.

prior to the first sample date; Columns 5 and 7 show the similar estimates when no such prior intake is assumed. It is apparent that the three methods frequently differ by as much as a factor of two, and in a few cases the differences are as great as a factor of three or four. It is not clear which method is to be preferred nor what are the major sources of error.

This paper discusses briefly some of the principal assumptions used in PUQUAE and suggests the degree of uncertainty that might be attributed to each. The study is to be regarded as suggestive rather than as definitive and cannot claim to be exhaustive. However, five possible sources of error are indicated and discussed.

Computational errors

These are errors due to round-off or to various approximations made in coding the problem. PUQUAE is mathematically rigorous if the metabolic model is granted. The effect of round-off and various approximations used is trivial.

Continuous model vs. discrete model

The hospital patients whose data are the basis of the model received a single intravenous injection. Intake by employees more likely will be continuous, whether the plutonium reaches the blood after inhalation or by ingestion. Likewise, excretion, if considered as excretion into the bladder, is perhaps better represented as a

1169805

continuous function rather than as a discrete process. Several experiments[4,5] have indicated that continuous exposure may be adequately considered as the integral of the single exposure model. Although this has not been demonstrated for Pu^{239}, it is probably not a major source of error.

The PUQUAE code uses the power function $at^{-\alpha}$ as governing the rate of excretion, although the constants a and α were obtained by fitting the curve to the discrete data representing daily excretion of Pu^{239}. This anomaly might be a considerable source of error during the early period, when the excretion rate is changing rapidly. Fig. 2 illustrates the principle involved. A hypothetical excretion rate curve is shown, together with a few assumed sample values. The values, if normalized to successive 24 hr periods should be compared to the shaded areas and not to the height of the curve on the date of the sample. The formulae given in Fig. 2 indicate

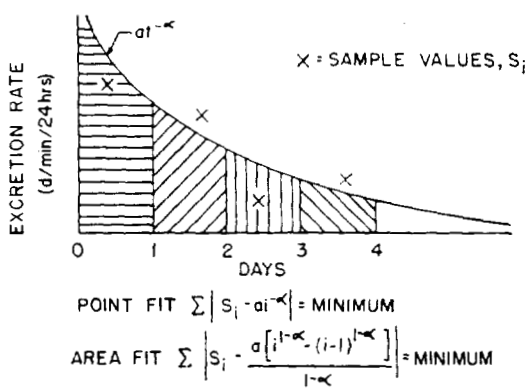

FIG. 2. Point fit and area fit of excretion data.

the two kinds of fit to the data, when the comparison is with point values or with area values. The formulae indicate that the sum of deviations is to be minimized, but one also may consider choosing a and α to minimize the sum of the squares of the deviations or the sum of the percentage deviations, etc. These latter types of fittings are being tried, but the complete results are not now available. Table 2 shows the values of a and α obtained by a least-squares fit of the curve heights to the points, and the same parameters when the area fit to the data is used. It will be noted that many of the values of α obtained by the point fit exceed 1, and this makes it impossible to use the value because it predicts an infinite excretion on the first day. No such anomaly has occurred when the area fit was used, although some difficulties with the code were encountered in two of the cases, and they are not yet resolved. For the cases with α less than 1, the intake has been estimated, and the percentage errors are generally smaller when the values obtained by the area fit are used. Thus it seems likely that the use of the Langham excretion curves may not be the best choice for PUQUAE, which requires an excretion rate curve rather than discrete daily outputs. It should be noted that Langham is in no way responsible for the misuse of his curves and that the discrete model may be the more appropriate one to use with PUQFUA, i.e. LAWRENCE's code.

Individual variation

The values of a and α in Table 2 differ considerably from one individual to another and the individual variation persists whatever method of fitting is used. We must conclude that, insofar as this evidence is concerned, there is significant individual variation. A considerable source of error in the estimates shown in Table 1 is probably due to this real difference of individuals. Table 3 shows the estimated intakes obtained in each case. When individual differences are taken into account, the error of the estimate is well below a factor of two. For some reason, as yet unexplained, the method of minimizing the sum of deviations seems to give a more accurate estimate than does the fit by least squares. However, even the estimates using a least-squares fit are not as large as the differences indicated in Table 1, and we must conclude that individual variation is probably a major source of error.

Frequency of sampling

Reference 2 indicated that the spacing of sample dates about hypothetical intakes might easily produce differences of as much as a factor of two in the estimates. These were hypothetical cases, and thus the adequacy of the model was not involved. Table 4 shows a partial check of this source of error, using the data of the hospital patients. The estimated intakes are shown when all excretion data are used, when only values on alternate days are used, and when data for every

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Table 2. Individual retention functions

Case	Least squares (point fit)		Least deviations (area fit)		Least squares (area fit)	
	a	α	a	α	a	α
Hp 1	0.2603	0.811	0.1050	0.422	0.1188	0.416
Hp 2	0.6843	1.224	0.1733	0.633	0.2090	0.581
Hp 3	0.4799	1.171	0.1645	0.711	0.2069	0.645
Hp 4	0.6871	1.081	0.2200	0.500	0.2281	0.508
Hp 5	0.1898	0.844	0.1110	0.625	0.1218	0.599
Hp 7	0.3926	1.201	0.0797	0.633		
Hp 8	0.3352	0.832	0.1561	0.586	0.1780	0.556
Hp 9	0.1137	0.455	0.0950	0.406	0.0960	0.402
Hp 10	0.6009	1.137	0.1650	0.602	0.2119	0.535
Hp 12	0.1192	0.470	0.0844	0.383	0.0851	0.333

Average excretion (LANGHAM) $0.23t^{-0.77}$

Table 3. Estimates of intake

Case	Injection (μc)	Estimated intake (average model)		Estimated intake (least-squares point fit)		Estimated intake (least-squares area fit)		Estimated intake (least deviations area fit)	
		μc	error (%)	μc	error (%)	μc	error (%)	μc	error (%)
Hp 1	0.283	0.174	−38.5	0.144	−48.1	0.224	−26.3	0.256	−9.5
Hp 2	0.314	0.239	−23.9			0.219	−43.4	0.293	−6.7
Hp 3	0.302	0.199	−34.1			0.217	−39.1	0.284	−6.0
Hp 4	0.302	0.293	−3.0			0.222	−36.0	0.225	−25.4
Hp 5	0.314	0.141	−55.1	0.148	−52.9	0.265	−18.5	0.295	−6.0
Hp 7	0.388	0.187	−51.8					0.487	+25.4
Hp 8	0.401	0.344	−14.2	0.227	−43.4	0.320	−25.3	0.394	−1.8
Hp 9	0.388	0.249	−35.8	0.369	−4.9	0.382	−1.6	0.393	+1.4
Hp 10	0.376	0.310	−21.3			0.265	−29.5	0.388	+3.1
Hp 12	0.289	0.242	−16.3	0.331	+14.5	0.326	+11.3	0.383	+32.5

third day are used. The effect is not large in these cases, but it seems likely that other patterns will produce a greater change in the estimates. Omitting one or more of the early samples would probably produce a greater change, and this is being tried.

Adequacy of the power function model

The adequacy of the power function as a model for the excretion of Pu^{239} has not been tested directly, but the percentages of error indicated in Table 3 do not seem great enough to require another model. It must be noted, however, that these tests extend over only some 140 days; a longer period might require another model.

In conclusion, the present tests suggest that with proper use of a continuous rate of excretion curve determined for the individual, and with frequent sampling, the intake of Pu^{239} to blood can be estimated within some 25 per cent. It is also suggested that with greater sampling intervals and when individual differences are neglected, the errors will be much greater, a

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Table 4. Effect of sample spacing on estimated intake

Case	Least deviations (area fit)		Daily samples		Alternate day		Every third day	
	a	α	Estimate	Error (%)	Estimate	Error (%)	Estimate	Error (%)
Hp 1	0.1050	0.422	0.256	−9.5	0.259	−8.5	0.249	−12.0
Hp 2	0.1733	0.633	0.293	−6.7	0.310	−1.3	0.309	−1.6
Hp 3	0.1654	0.711	0.284	−6.0	0.298	−1.2	0.347	+14.9
Hp 4	0.2200	0.500	0.225	−25.4	0.247	−18.1	0.249	−17.5
Hp 5	0.1110	0.625	0.295	−6.0	0.301	−4.1	0.334	+6.4
Hp 7	0.0797	0.633	0.487	+25.4	0.476	+22.7	0.486	+25.3
Hp 8	0.1561	0.586	0.394	−1.8	0.393	−2.0	0.426	+6.2
Hp 9	0.0950	0.406	0.393	+1.4	0.398	+2.6	0.412	+6.2
Hp 10	0.1650	0.602	0.388	+3.1	0.393	+4.5	0.417	+10.9
Hp 12	0.0844	0.383	0.383	+32.5	0.344	+19.0	0.420	+45.3

factor of two being common. This is rather disturbing for applied health physics, because very frequent sampling is impractical and there is no theory available to correct for individual differences. It is necessary to remember that the foregoing statements are suggestions only, and that they rest on relatively few cases observed over a fairly short period of time and with the simplest of intake patterns. It is clear that we still are not able to predict an employee's body burden within a factor of less than two under actual conditions of employment.

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