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FLUCTUATIONS OF DAILY EXCRETION OF PLUTONIUM AND THEIR INTERPRETATION FOR ESTIMATION OF THE BODY BURDEN*

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The Minimum Detectable Amount (MDS) of ^{239}Pu may be discussed from several points of view, all of which have some relevance to the problem of protection or monitoring of plutonium workers. On the one hand, one might be concerned with the sensitivity of analytical methods for plutonium present in urine or in feces; but, important though it may be for the overall problem, that is not the subject of this paper. Rather, we wish to consider here the question of how one can distinguish a high level in urine due to a new intake from a high level that is merely a result of the

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day-to-day fluctuations of urinary excretion. That such daily fluctuations exist is well documented, for example, in the classical studies of Langham.[1] The distribution of these excretion values has been studied by three of the present authors.[2] Beach and Dolphin[3] also have studied the distribution of excretion values for a group of occupationally exposed subjects with rather similar results. That is to say, high excretion values—and low excretion values too—seem to occur with a certain frequency which we consider here as occurring by chance, but with a distribution which is approximately known. The problem then is the following: How can one distinguish a high urine level which is only a sporadic high value, one due to a "chance fluctuation," from a high value due to a new intake of plutonium? Of course, one answer is easy: Collect additional samples and thus determine whether the excretion now fluctuates about the old level or at a higher level. No doubt, that is the "conservative" answer, but it does involve collecting and analyzing quite a few samples.

Let us be clear in stating the problem that we are not presupposing an "incident" or unusual occurrence in the work record of the employee. If there is such an "incident" and attendant suspicion of intake of plutonium, then one must collect sufficient samples to assess properly the probable amount of this supposed intake. Rather, we consider here the employee with potential exposure to plutonium who is being routinely sampled but without any immediate and special reason for suspecting a recent intake. An occasional sample will be high just because fluctuations do occur. Is there any plausible basis for deciding whether one should collect more samples in

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attempting to decide whether a new intake has occurred? Let it be said at once that our consideration of this problem is only preliminary.

The problem may be formulated as follows: Suppose an employee has a chronic body burden of 1 unit so that his excretion may be considered as somewhat comparable to that of the terminal patients studied by Langham when their data are normalized to unit intake to blood. Let $y(t)$ be the excretion predicted t days postintake according to Langham's formula or any similar formula; the actual excretion values $U(t)$ will fluctuate about the predicted values, and only if they are exceptionally high—say, by some factor S—would one consider that a new intake had occurred; and finally, let I be a supposed new intake which occurs on some day j prior to t. Then the total urine output on day t should satisfy

$$I\,U(t-j) + U(t) \geqq S\,y(t) \tag{1}$$

if the new intake will be noticed. The two terms on the left member represent the excretion due to the recent intake on day t-j and that due to the chronic burden, respectively, and the inequality is interpreted to mean that only in case the excretion is significantly high will a new intake be investigated. In this paper, we explore in a preliminary way the practical implications of the use of such a level of significance with this interpretation.

In Fig. 1 the distribution of fluctuations about the excretion model $y(t)$ is shown for one case, namely, where

$$y(t) = \int_{t-1}^{t} b\tau^{-\alpha}\,dt = \frac{b}{1-\alpha}\left[t^{1-\alpha} - (t-1)^{1-\alpha}\right]. \tag{2}$$

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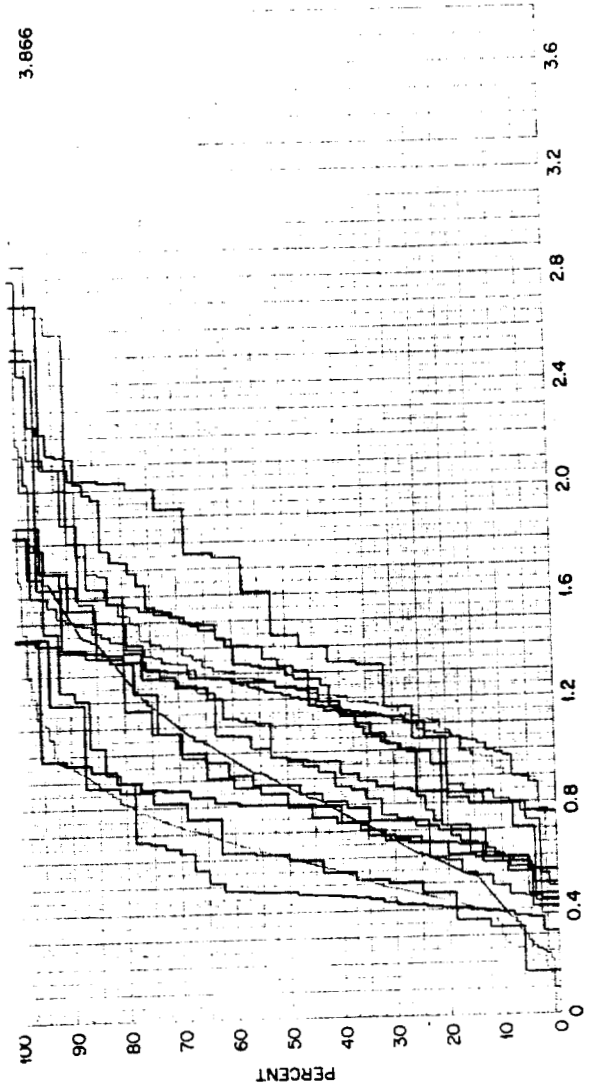

Fig. 1. Fluctuations of Daily Urinary Excretion Data of all Patients (Langham—1950) about the Typical Formula of Best Fit—"Area Fit" Formula Obtained by Minimizing the Sum of Absolute Deviations.

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As reported in reference 2, this formula has been fitted to the excretion data of all the hospital patients to minimize the sum of percent deviations, thus obtaining the values $b = 0.0015$ and $\alpha = 0.65$. One could use a number of other formulas in place of this one, but the results do not seem to be much different. The cumulative distribution of the ratios $U(t)/y(t)$ has been plotted in Fig. 1 for each of the hospital patients. Also only the smallest region including all these curves is shown. It is seen, for example, that the ratio $U(t)/y(t)$ may exceed 2.59, but not for more than 10% of the sample values of any one patient, and, likewise, it might be expected to exceed 2.03 for 20% of the samples in some cases. The significance factor S will be chosen from this graph; that is, a value of $S = 2.6$ represents a significance level such that no hospital patient had more than 10% of the sample values higher than $2.6\ y(t)$. We term this a 90% significance level. Likewise, the values $S = 2.0$, $S = 1.9$, and $S = 1.4$ are significance levels of 80%, 70%, and 50%, respectively.

In this paper we consider the probability of the additional excretion due to an intake I being "significantly" high in the sense that inequality[1] is satisfied, and we examine this as a function of the sampling time. Thus, supposing $j = t-1$ (That is, that the hypothetical intake for a certain patient occurred one day before the beginning of the sampling day), the additional excretion to be expected, IU_1, is taken from the excretion data of that hospital patient. The supposed day of intake in relation to the sampling day is varied. Thus in (1) we choose $t = 31, 32\ldots, 40$ and always take $j = t-1$. Doing this for all the patients, one has a total of at most 120 possible cases. In Fig. 2 we

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show that results for I = 1 when sampling occurs j days postintake for j = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 18, 26 days prior to the close of the sampling period. Three curves are shown for t in the ranges 31-60 days, 61-100 days, and 101-140, respectively. In all cases the additional excretion was significantly high, i.e., by a factor of 2.6 more than expected by the formula if sampling occurred within a few days of the intake. However, the probability of being above the significance level decreases rapidly as sampling is postponed. Because these curves did not differ significantly, the results were pooled for t ranging from 31-140 days or to the death of the patient.

In Fig. 3 we show how the probability of detection varies as I is decreased. It will be noted that the curves rapidly approach zero as I is decreased. Thus we must conclude that one cannot distinguish additional excretion from normal fluctuations at the 90% level of significance (S = 2.6) except for a few days postexposure even when the intake amounts to the body burden of the employee. At lower levels of intake, the probability is generally small that the "intake" would be noticed.

In Fig. 4 the corresponding results are shown for the 80% level of significance, that is, S = 2.0. Although the probability of being considered significant is near 1 for a somewhat longer period than is true at the 90% level, nevertheless, the curves quickly decrease. Thus the former pessimistic conclusion is confirmed. One cannot distinguish intakes which amount to 10% to 100% of the body burden unless sampling occurs soon after the intake. Figures 5 and 6 contain the corresponding results for significance levels of 70% and 50%, respectively, and while the

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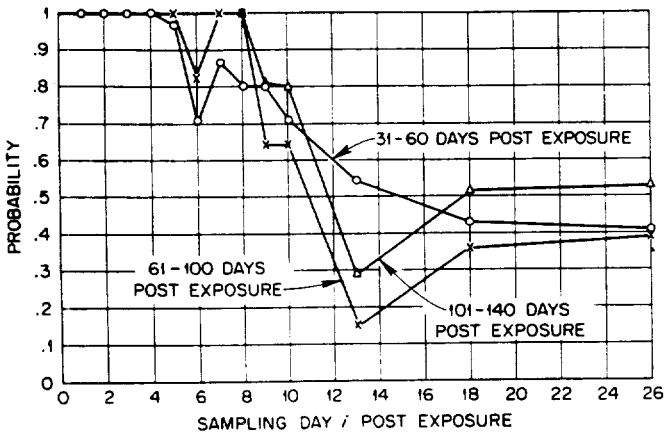

Fig. 2. Probability of Observing α New Intake, I = 1; Significance Level—90% for Different Ranges of Chronic Exposure.

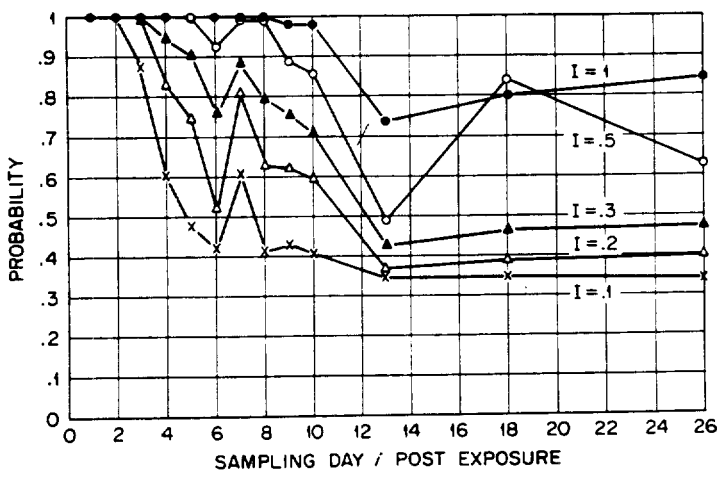

Fig. 3. Probability of Observing a New Intake, I; Significance Level—50%.

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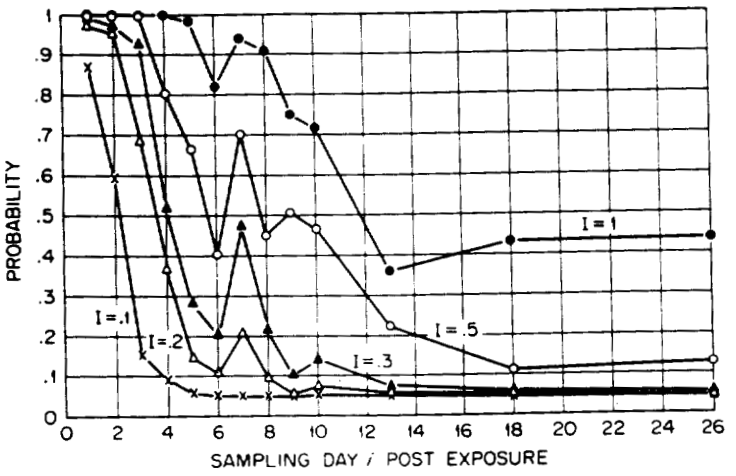

Fig. 4. Probability of Observing a New Intake, I; Significance Level—90%.

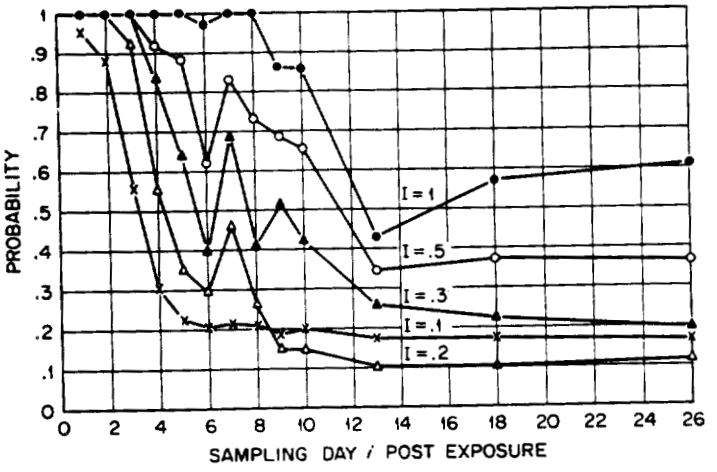

Fig. 5. Probability of Observing a New Intake, I; Significance Level—80%.

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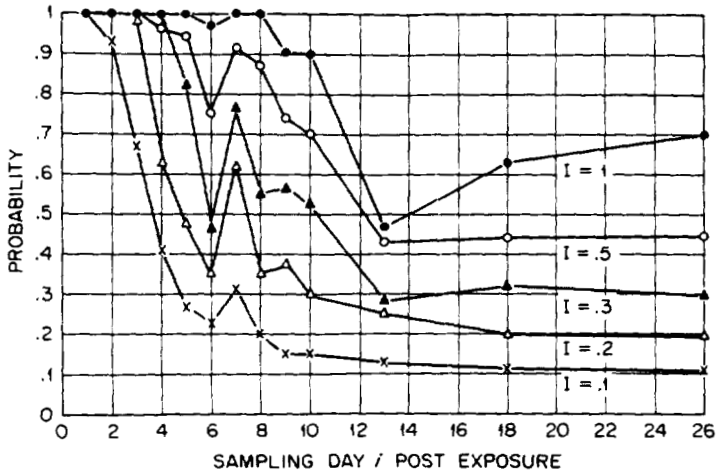

Fig. 6. Probability of Observing a New Intake, I; Significance Level—70%.

results are somewhat better, they do not support the view that sampling once a month is sifficiently frequent for a routine monitoring program. If one lowers the level of significance, one will be investigating many high values which are mere fluctuations, and if one uses a high level of significance, one cannot distinguish intakes of the order of the employee's present body burden.

Of course, one may raise numerous objections to the procedure studied here. The hospital patients were terminal patients, and the administered plutonium was complexed with citrate, and so their excretion patterns may not be those of employees. Certainly one would like to have other data, but other than the data on employees whose intake is largely indeterminate, this is all we have. Moreover, the distribution of fluctuations as analyzed by Beach and Dolphin does not differ markedly from that used here. This

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study assumes that the fluctuations of excretion due to the recent intake and for the excretion due to the chronic burden are uncorrelated. It is possible that they are correlated, and we plan to explore the implications of this in another study. We can only conclude that a sampling frequency of once a month does not suffice to detect new intakes of, say, 50% or less of the body burden with a high probability. It seems necessary to follow each high value by one or more resamplings with the expectation that many of them will be rejected finally as merely spurious "high" fluctuations of the daily excretion.

Beach et al.[4] have suggested that a program of pooled samples affords a better basis for a monitoring program. Therefore, we are undertaking a study of the effects of such pooling. In Fig. 7 are shown the cumulative curves corresponding to pooled samples extending over five days. As will be noted, these cumulative distributions are somewhat more narrowly grouped about 1 and thus should afford a somewhat better basis for a monitoring program. We plan to explore the implications of this procedure in another paper.

We are exploring other uses of these data, particularly when more than one sample is obtained. For example, we were asked to study a case arising from a contaminated wound. After a period of treatment with DTPA, the excretion pattern fit well within the pattern of fluctuations found here. Thus if plutonium were leaching from the wound, the amounts were too small to produce an excess of high values. We cannot prove with finality that transport of material was not occuring; however, one can say that the data are compatible with hypothesis of no significant

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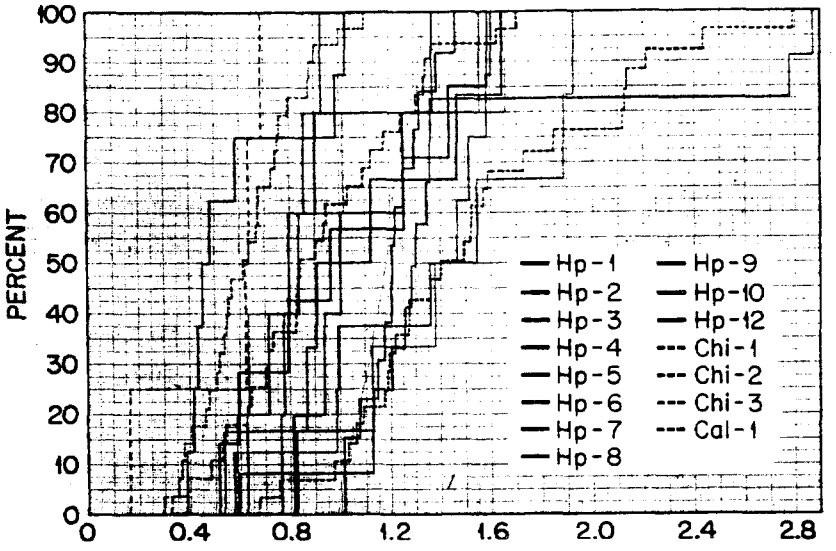

Fig. 7. Fluctuations of Pooled Daily Urinary Excretion Data (5 days) of all Patients (Langham—1950) about the "Typical" Formula of Best Fit—"Area Fit" Formula Obtained by Minimizing the Sum of Absolute Deviations.

transport. Further details of this analysis are reported in our annual progress report for 1968.[5]

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