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ON THE ESTIMATION OF A SYSTEMIC BODY BURDEN OF PLUTONIUM*

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Abstract — Résumé — Аннотация — Resumen

ON THE ESTIMATION OF A SYSTEMIC BODY BURDEN OF PLUTONIUM. Several computer programmes have been described in the literature which use the complete urinalysis record of employees to estimate their systemic body burden of plutonium-239, i.e. the body burden exclusive of plutonium-239 in the lungs or in the contents of the gastro-intestinal tract. For each successive sample date such codes use an excretion model, suggested by Langham, to estimate the urinary excretion that would be expected to result from prior intakes that have been estimated. Any excess in the sample is considered to indicate an additional intake, or is rejected as being the result of an erroneous determination. An examination of excretion data taken under controlled conditions indicates that there is considerable fluctuation about the smoothed curves used in the excretion model, that the deviations are by less than a factor of two in the majority of cases, and that much of this fluctuation must be accepted as of biological origin and not merely the result of faulty sampling techniques. This suggests that a mathematical treatment should accept small fluctuations as not necessarily indicating additional exposure or artifacts of sampling. Such a computer code has been written and tested on the few cases where the body burden is considered to be well established. These cases suggest that this technique may be an improvement over earlier methods. The code uses one index as specifying a level below which data are not considered to be significant, and a second index specifies the degree of excess over the general trend which is considered to be due to additional intake to blood.

ÉVALUATION D'UNE CHARGE CORPORELLE SYSTÉMIQUE DE PLUTONIUM. On trouve, dans des publications spécialisées, la description de plusieurs programmes de calculatrices qui, d'après les résultats complets d'analyses d'échantillons prélévés sur les urines de travailleurs, permettent d'évaluer chez ces derniers la charge corporelle systémique de plutonium 239, c'est-à-dire la charge corporelle à l'exclusion du plutonium 239 présent dans les poumons ou dans le contenu du tractus gastro-intestinal. Pour chacune des dates de prélèvement successives, les codes sont fondés sur un modèle d'excrétion, suggéré par Langham, qui permet de prévoir l'excrétion dans les urines à laquelle on peut s'attendre, à la suite d'absorptions antérieures de quantités estimées. Tout excédent dans l'échantillon est considéré comme dénotant l'absorption d'une quantité supplémentaire, ou écarté comme étant le résultat d'une détermination érronée. Les constatations suivantes ressortent de l'examen sous contrôle des données relatives à l'excrétion de plutonium: il existe des variations considérables de part et d'autre des courbes ajustées utilisées dans le modèle d'excrétion; les écarts sont, dans la plupart des cas, de l'ordre d'un facteur inférieur à deux; les variations ne sont pas dues simplement à l'imperfection des techniques de prélèvement, mais doivent en grande partie être attribuées à une cause biologique. Pour traiter ce problème mathématiquement, il faut donc admettre, semble-t-il, que de faibles variations n'impliquent pas nécessairement une exposition supplémentaire ni un phénomène artificiel qui serait la conséquence du prélèvement d'échantillons. Sur cette base, on a élaboré un code pour calculatrices, dont on a fait l'essai sur les quelques cas où la charge corporelle est considérée comme connue. Il ressort de ces cas que cette méthode peut constituer une amélioration par rapport à celles qui étaient appliquées auparavant. Dans le code ainsi élaboré, un indice définit le niveau en dessous duquel les données ne sont pas considérées comme significatives et un autre indice définit la valeur excédentaire par rapport à la tendance générale, qui est considérée comme impliquant une absorption supplémentaire de plutonium dans le sang.

ОБ ОПРЕДЕЛЕНИИ СОДЕРЖАНИЯ ПЛУТОНИЯ В СИСТЕМАХ ОРГАНИЗМА. В литературе уже были описаны различные счетно-вычислительные программы, использующие полные данные анализа мочи рабочих для определения содержания плутония-239 в системах ор-

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ганизма, например только в легких или в содержимом желудочно-кишечного тракта. Для каждой последующей пробы в таких кодах используется модель выделения, предложенная Лангхэмом, для определения ожидаемого количества выделения с мочой после первичного всасывания, которое было подсчитано. Любое повышение уровня изотопа в пробе рассматривается на дополнительное всасывание или отбрасывается как результат ошибочного определения. Изучение данных выведения, полученных в контролируемых условиях, показывает, что имеется значительная флуктуация вне выпрямленных кривых, используемых в моделях выведения, что такое отклонение имеет по крайней мере коэффициент 2 в большинстве случаев и что большая часть такой флуктуации имеет биологическое происхождение, а не является результатом ошибочной методики взятия проб. Из этого следует, что математическая обработка допускает небольшие флуктуации как необязательно указывающие на дополнительное облучение или артефакты при взятии проб. Подобные счетно-решающие коды были составлены и опробованы в нескольких случаях, когда считалось, что содержание радиоизотопов в организме может быть точно установлено. Эти случаи доказывают, что данный метод может считаться более совершенным, чем ранее применявшиеся.

В этом коде употребляется один индекс, определяющий уровень, ниже которого показатели не имеют значения, а второй индекс точно указывает степень избытка сверх общей тенденции, что рассматривается как результат дополнительного поглощения в крови.

EVALUACIÓN DE LA CARGA GENERAL DE PLUTONIO. Se han descrito en la literatura especializada varias claves de cómputo que utilizan los resultados completos del análisis de orina para calcular la carga general de plutonio-239, esto es, la carga corporal con exclusión del plutonio-239 presente en los pulmones o en el contenido del tracto gastrointestinal. Para cada fecha sucesiva de muestreo, dichas claves aplican un modelo de eliminación por excreción, propuesto por Langham, para calcular la excreción urinaria que resultaría de absorciones anteriores ya evaluadas. Todo exceso en la muestra se considera como indicio de una nueva absorción, o se desprecia por estimarse resultado de una determinación errónea. El examen de los datos relativos a la excreción, obtenidos en condiciones controladas, muestra que las curvas corregidas que se utilizan en el modelo de eliminación por excreción, acusan considerables fluctuaciones, que en la mayoría de los casos las desviaciones son inferiores al 200%, y que debe aceptarse que muchas de estas fluctuaciones tienen un origen biológico y no son meramente resultado de técnicas de muestreo defectuosas. Ello indica que al aplicar un tratamiento matemático debe aceptarse que las pequeñas fluctuaciones no suponen necesariamente una exposición adicional ni artificios en la técnica de muestreo. Dicha clave de cómputo se ha preparado y probado en los pocos casos en que la carga corporal se consideraba bien conocida. Tales casos parecen indicar que esta técnica puede constituir un perfeccionamiento respecto de métodos anteriores. En la clave se utiliza un índice que define un nivel por debajo del cual los datos no se consideran significativos; un segundo índice define el grado de exceso sobre la tendencia general que se considera debido a absorción sanguínea adicional.

Internal exposure to plutonium, particularly Pu^{239}, poses an important and difficult problem for the health physicist. No techniques of whole-body gamma detection have been devised that are sensitive enough to measure a systemic body burden at the maximum permissible level recommended by the International Commission on Radiological Protection (ICRP), and thus those charged with evaluating an employee's exposure must attempt to base this evaluation on interpretation of such data on excretion of the radionuclide as may be available. Whether the exposure is acute or chronic and whether the plutonium entered the body by inhalation, by ingestion, or through a wound, the problem posed is one of the most difficult for the health physicist.

Several computer codes which use an employee's urinalysis data to estimate his systemic body burden of Pu^{239} have been described in the literature [1, 2]. These codes and other similar ones designed by the author are based on the metabolic model devised by LANGHAM to represent the excretion and retention in man following intravenous administration of Pu^{239} [3]. Briefly, Langham analysed the excretion data of some eleven terminal patients

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who received injections of Pu^{+4}-citrate. He found that power functions described the general trend of the excretion data during some 138 d. By ingenious analysis he was able to indicate that probably the same functions were adequate to represent the trend of excretion data of employees over periods of five years or longer. However, the hospital cases as well as the data on employees show a considerable degree of fluctuation about the curves describing the trend of the data.

The author has designed a code which, to some extent, takes into account possible fluctuations about the trend of the data. Assuming S_i is the measured amount of Pu^{239} in urine on day t_i $i = 1, 2, \ldots, n$, the problem consists of determining intakes I_i of Pu^{239} to blood which will account for the excretion record and be consistent with the metabolic model. The model is represented by a series of constants U_j, each U_j being the fraction of dose of Pu^{239} to blood which is excreted in the urine j days later. The constants U_j may be computed by a formula or may be entered in the code as a table of constants.

The computer first selects a time j_1 preceding the first sample day t_1 and computes the first intake

$$I_1 = S_1 / U_{t_1 - j_1}.$$

Thus the first sample value is accounted for exactly by I_1. The intake I_1 already produces urinary excretion

$$I_1 U_{t_i - j_1}$$

on day t_i, and so the computer calculates reduced excretions

$$S'_i = S_i - I_1 U_{t_i - j_1}, \quad i = 2, 3, \ldots, n.$$

Because of inaccuracies in the model or because of statistical fluctuations of the data, it may happen that some S'_i are negative. If this is the case, the machine will make a second choice of time j_1 for the first intake. In fact, the computer will systematically try all choices of day j_1 for the first intake and select that one as final choice which makes the negative values of the S'_i, if any, as large as possible, i.e. as close to zero as possible.

Having determined I_1 and j_1, the computer examines S'_2. If S'_2 is below a certain pre-assigned value which represents a reasonable estimate of expected fluctuations of the data about the trend, the computer will ignore S'_2 and consider that no new intake is required. If S'_2 exceeds the pre-assigned level of significance, a second intake is computed, the day j_2 of this intake being restricted to lie between the dates of the first and second samples. Proceeding serially, the computer estimates all the intakes required to produce the urine data according to the model. In principle, this code is essentially the same as that of LAWRENCE [1] but does not reject data points and does allow for some flexibility in choosing the times for the intakes to blood and in disregarding certain fluctuations of the data as not being significant.

To test the code, data on dogs exposed to Pu^{239} at Hanford Biology Laboratory have been used [4]. BAIR et al. injected three dogs with plutonium

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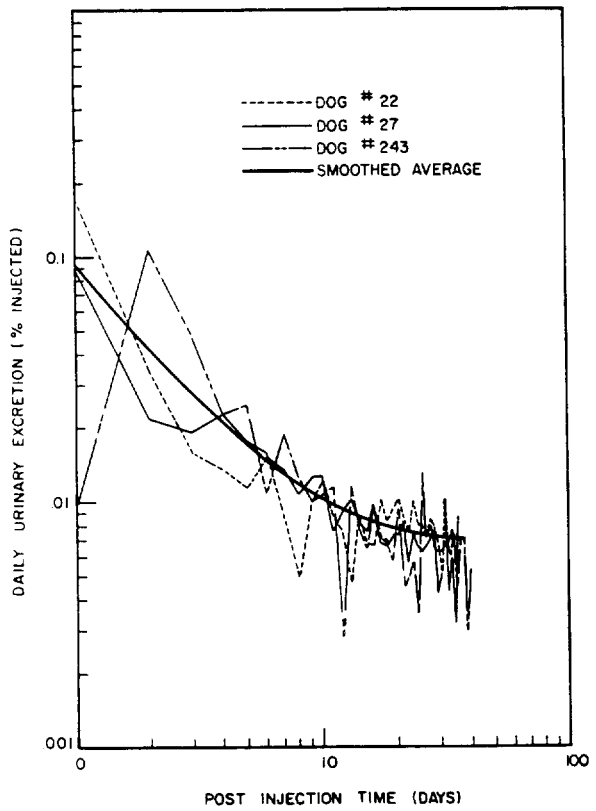

Fig. 1

Urinary excretion following intravenous injection of plutonium nitrate

nitrate (0.14 N HNO_3), and the dogs were sacrificed ~30 d post-injection. The urinary excretion data are plotted in Fig. 1 together with a curve representing an average of the data. It is apparent that there are very wide fluctuations from day to day and that the dogs differ rather markedly so far as day-to-day excretion is concerned. Nevertheless, the code mentioned above was used to estimate the intake. In Fig. 2 the daily intakes as estimated by the code are shown in the form of a bar histogram. It is clear that, despite the erratic character of the excretion data, the code did correctly find that the intake was confined largely to the first day or two. The small intakes to blood on succeeding days are the result of unusually high fluctuations of the excretion data. Thus the code did give a qualitatively correct interpretation so far as time of intake is concerned. The estimated total intake is shown together with the injected amount, and it is evident that the estimates are within a factor of 2. In view of the erratic character of the data, this is considered to be encouraging.

BAIR et al. [4] also exposed dogs by inhalation, some to plutonium nitrate (0.14 N HNO_3) and others to Pu^{239} O_2. The urinary excretion data of those dogs exposed to the nitrate were analysed by the code also, and the

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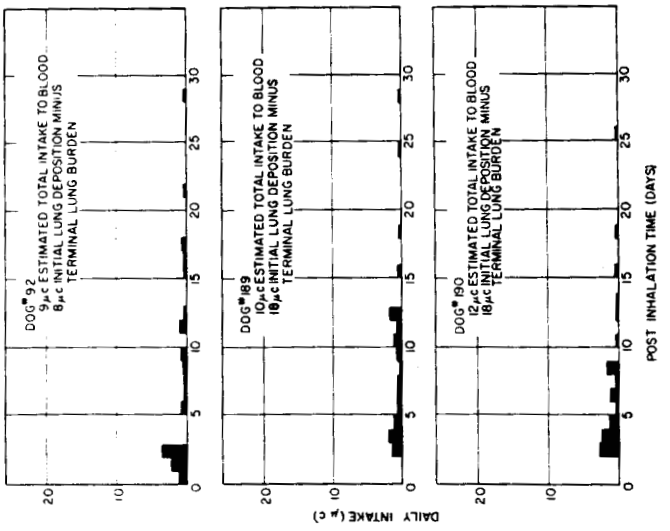

Fig. 3

Computer estimates of intake to blood. Inhalation cases.

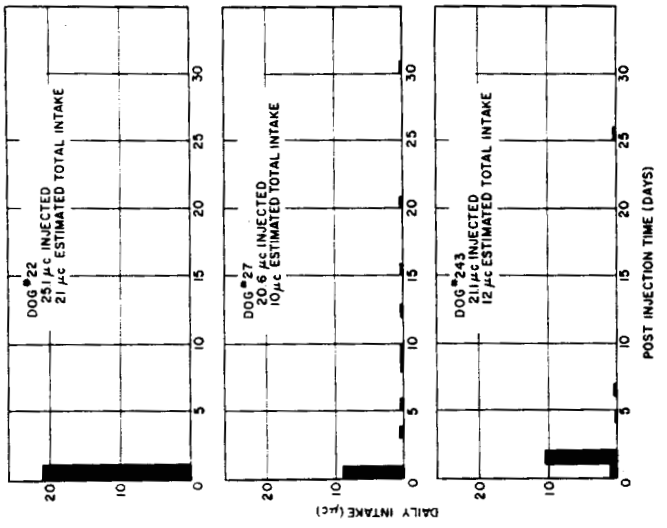

Fig. 2

Computer estimates of intake to blood. Single intravenous injection cases.

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estimated intakes to blood are shown in Fig. 3. Although the time sequence is erratic, significant intakes to blood do seem to occur over a succession of days and tend to decrease with time. Thus the qualitative aspects are as we might expect. However, the large number of days of no intake undoubtedly is an artifact produced by sporadic high excretions early in the period of observation. The estimated total intake to blood is shown also on Fig. 3 together with the difference of lung deposition and the terminal lung burden as estimated by the experimenters. Again the results generally agree within a factor of 2.

It seems clear that the present methods cannot be relied upon to give more than a very rough indication of the intake to blood. There are a number of possible improvements that suggest themselves. Some preliminary smoothing of data, perhaps by the computer, might reduce the error. However, it seems likely that marked improvements will come only with a better understanding of the metabolic model and of the probable source of the wide individual differences and day-to-day fluctuations of the excretion data. It would seem that carefully controlled experiments might help in understanding these difficulties and that even if the experiments did not enable us to overcome these difficulties, we might in this way obtain a firmer estimate of the uncertainty of our method of estimation.

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REFERENCES

[1] LAWRENCE, J.N.P., Health Physics 8 1 (1962) 61-6.
[2] SNYDER, W.S., ANL-6673, p.13.
[3] LANGHAM, W.H. et al., LA-1151 (20 Sept., 1950).
[4] BAIR, W.J. et al., Health Physics 8 6 (1962) 639-49.

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