Human exposure to natural uranium

A case history and analytical results from some postmortem tissues

J. K. DONOGHUE¹, E. D. DYSON², J. S. HISLOP, A. M. LEACH³,
and N. L. SPOOR²

United Kingdom Atomic Energy Authority, Harwell, Didcot, Berks and
Risley, Warrington, Lancs.

Donoghue, J. K., Dyson, E. D., Hislop, J. S., Leach, A. M., and Spoor, N. L. (1972). *Brit. J. industr. Med.*, 29, 81-89. **Human exposure to natural uranium: a case history and analytical results from some postmortem tissues.** After the collapse and sudden death of an employee who had worked for 10 years in a natural uranium workshop, in which the airborne uranium was largely U_3O_8 with an Activity Median Aerodynamic Diameter in the range 3.5-6.0 μm and average concentration of 300 $\mu g/m^3$, his internal organs were analysed for uranium. The tissues examined included lungs (1041 g), pulmonary lymph nodes (12 g), sternum (114 g), and kidneys (217 g). Uranium was estimated by neutron activation analysis, using irradiated tissue ash, and counting the delayed neutrons from uranium-235. The concentrations of uranium (μg U/g wet tissue) in the lungs, lymph nodes, sternum, and kidneys were 1.2, 1.8, 0.09, and 0.14 respectively. The weights deposited in the lungs and lymph nodes are less than 1% of the amounts calculated from the environmental data using the parameters currently applied in radiological protection. The figures are compatible with those reported by Quigley, Heatherton, and Ziegler in 1958 and by Meichen in 1962. The relation between these results, the environmental exposure data, and biological monitoring data is discussed in the context of current views on the metabolism of inhaled insoluble uranium.

Several investigators have discussed the deposition of uranium in the human lung following exposure to 'insoluble' uranium. Quigley *et al.* (1958) have presented analytical results from tissues obtained from three necropsies. The deaths were unrelated to occupation, and the amounts of uranium in the lungs and kidneys were unexpectedly small. Two subjects had been exposed for a few years to low concentrations of relatively insoluble uranium and the uranium concentrations in the lung (μg U/g wet tissue) were 0.4 and 1.0. Although these figures are

high in relation to the controls (0.001 $\mu g/g$) they are low in relation to the deposited amounts estimated from the levels of exposure. The value of Quigley's paper is limited by the inadequacy of the environmental data, which included no detailed information about particle size.

Some of the 26 cases in which significant human chest burdens have been reported in detail involved retained uranium which was partly enriched (i.e., in which the proportions of ^{234}U and ^{235}U exceed those in natural uranium). In three of the cases reported, the uranium deposited was probably in the form of U_3O_8 . In the other cases the uranium may have been in the form of U_3O_8 , or UO_3 , or some other uranium compound or mixture of compounds. Fish and Patterson (1958) and Fish (1961) refer to 'uranium fume' and Saxby and his colleagues (1964

¹Present address: British Nuclear Fuels Limited, Risley, Warrington, Lancs.

²National Radiological Protection Board, Harwell, Didcot, Berks.

³Medical Department, Wilton Works, Imperial Chemical Industries Limited, Eston, Middlesbrough, Yorkshire.

to 'enriched uranium dust, probably in the form of the insoluble oxide U_3O_8 '. Scott and West (1964) and West and Scott (1969) are unavoidably less precise. One of their subjects worked in an area 'where exposure materials include such highly insoluble uranium as high-fired uranium oxides, uranium ceramics, and certain uranium metal alloys'. Another subject worked in an area 'where the most probable exposure material was uranium oxide or metal'. Schultz (1966) refers to the importance of giving 'careful consideration to the physico-chemical characteristics of the particles' and to the relative insolubility of the uranium oxides, especially U_3O_8 . In the case history reported by Ronen (1969), the employee 'had been engaged in recovering uranium alloy scrap from graphite moulds'. In their report on the retention of uranium by 15 persons who had been chronically exposed to 'non-transportable' uranium oxides, Quastel, Taniguchi, Overton, and Abbatt (1970) describe the airborne dusts as 'uranium dioxide' in one part of their paper and in another as 'uranium oxide dusts'. In most of the investigations summarized in Table 1 the information concerning the physical and chemical characteristics of the inhaled uranium is inadequate to support any interpretation aimed at relating exposure data to retention data.

The instrument used for obtaining the chest burden data listed in Table 1 is the whole body

monitor, which can reliably detect in vivo 10 mg natural uranium or 1 mg enriched uranium. In measuring the half-life of uranium in the chest this equipment possesses only two disadvantages: it cannot measure accurately the small deposits (1 to 5 mg) in the chest occasionally associated with occupational exposure to natural uranium and it cannot distinguish between the uranium deposited in the lungs and that deposited in the tracheobronchial lymph nodes, the sternum, and the ribs. This emphasizes the desirability of obtaining analytical data from postmortem tissues related to a known exposure history.

Methods and results

The postmortem tissues

An employee, who up to the day of his death had worked in a uranium workshop for 10 years, died suddenly from natural causes. Because there was no postexposure period before death the postmortem data may be related to normal working conditions and also to his normal metabolism. After the necropsy certain tissues (two lungs, two kidneys, the sternum, and a sample of liver) were excised, placed in plastic bags, and kept in a deep-freeze cabinet. The recovery of the lungs and kidneys was complete. These tissues were later dissected by one of us (E.D.D.) and prepared for chemical analysis. At this stage the lymph nodes from the hilar region and main bronchi were separated from the tracheobronchial and lung tissues, and the lobes of the lung were separated. In

TABLE 1
HUMAN METABOLISM OF INSOLUBLE URANIUM

Investigator	Place	No. of exposed persons	Chest burden		Biological half-life (days)	Substance
			mg	nCi		
Miller (1957, 1958) .. McLendon (1959) .. Fish (1961) Fish and Patterson (1958)	Oak Ridge	1	3	30 ¹	21 and 121 (two mechanisms)	U_3O_8 (enriched)
Scott and West (1964) .. West and Scott (1969)	Oak Ridge	4	0.5-2.0	20-50	Range 550-1500	Uranium oxide, ceramic, or alloy ² (enriched)
Saxby <i>et al.</i> (1964) ..	Aldermaston Harwell	2	1 ¹	60	11 and 360 (two mechanisms)	Uranium oxide or silicate ² (enriched)
Schultz (1966) ..	Oak Ridge	4	0.02-1.0	1.0-30	Range 120-250	U_3O_8 (enriched)
Ronen (1969)	Negev	1	207	140	100 and 1200 (two mechanisms)	Uranium oxides and (probably) other uranium compounds (natural)
Quastel <i>et al.</i> (1970) ..	Ottawa	15	10-100	6-60	No information	UO_2 (natural)

¹Estimated value. ²Probably U_3O_8 .

addition, the kidneys were divided into cortical and medullary tissues.

Atmospheric contamination

The assessment of the overall environmental exposure of this employee to uranium during the period 1959-69 is based on:

- (a) the results of the (high volume) static air sampling (S.A.S.) programme followed throughout the period;
- (b) the results of measurements made in 1968 using personal air samplers of the type described by Sherwood and Greenhalgh (1960); and
- (c) more recent information about the nature of the airborne dust in the shop where he had worked.

(a) **Static air sampling** The S.A.S. programme was largely concerned with plant control and the sampling heads were deliberately placed in locations where release of dust was expected. For this reason many of the S.A.S. results cannot be used for determining the average exposure of an individual employee. These results do, however, definitely indicate that there has been no long-term trend, upwards or downwards, in the air contamination level.

(b) **Measurements made in 1968** During 1968 a short investigation with personal air samplers (P.A.S.) was carried out. As usual, the P.A.S. results indicated a higher air contamination level than did the S.A.S. results. For the individual concerned the average level was $390 \mu\text{g}/\text{m}^3$ and this was close to the average for all workers in the plant. This level is almost certainly too high; Butterworth and Donoghue (1970) have shown that a personal air sampler worn on the chest can pick up contamination, released from protective clothing, which does not necessarily enter the breathing zone. Making allowance for this factor, the long-term average exposure level is estimated to be about $300 \mu\text{g}/\text{m}^3$.

Particle size measurements made at the time of the P.A.S. investigation gave Activity Median Aerodynamic Diameters (A.M.A.D.) in the range $3.5\text{--}6.0 \mu\text{m}$. According to the International Commission on Radiological Protection (I.C.R.P.) Task Group on Lung Dynamics (1966), at these particle sizes deposition in the pulmonary compartment might be expected to be in the range 10-15 %, and deposition in the nasopharynx 70-80 % of the amount inhaled.

(c) **Measurements made in 1970** In August 1970 an attempt was made to investigate the composition of the airborne dust in the working area. About 30 g settled dust was collected from ledges between 3 and 10 metres above ground level. Tetrabromoethane (density $2.96 \text{ g}/\text{ml}$) was used to separate a lighter fraction from a heavier, and both fractions were passed through a 60 BSS sieve ($0\text{--}220 \mu\text{m}$). The results of an analysis of the heavier and lighter

fractions which passed the 60 BSS sieve are given in Table 2. This coarse settled dust contained about 75 % of uranium oxide; the other ingredients probably included aluminium oxide and calcium and magnesium silicates. The two fractions were examined by x-ray diffraction and it was estimated that in both cases 85 % of the uranium was in the form of U_3O_8 and the remainder as UO_2 . These analytical findings are incomplete in that they may not provide a reliable indication of the composition of the airborne dust of respirable size during the period 1959-69.

TABLE 2
ANALYSIS OF SETTLED DUST

Element	Light fraction ¹ (%)	Heavy fraction ² (%)
Uranium	14.3	70.4
Aluminium	7	10
Calcium	6	1
Magnesium	4	4
Silicon	8	1
Thorium	0.07	0.15
Zinc	0.5	1

¹Dust of density less than $2.96 \text{ g}/\text{ml}$ and passing the 60 mesh sieve (roughly $220 \mu\text{m}$).

²Dust of density more than $2.96 \text{ g}/\text{ml}$ and passing the 60 mesh sieve (roughly $220 \mu\text{m}$).

Urine analysis

The results of routine analyses of end-of-shift urine samples are given in Table 3. The concentrations of uranium were generally low; most of the figures were at a level of $20 \mu\text{g}/\text{l}$ or lower, and many were lower than the limit of detection ($5 \mu\text{g}/\text{l}$).

In June, July, and August 1968 an increased number of urine samples was analysed. The increased frequency in June was connected with an investigation in which an attempt was made to relate air contamination levels to excretion levels. The increased frequency in July and August was connected with an accident, in which the worker concerned received a wound of the right lower limb which became contaminated with uranium dust. The contaminated wound resulted in some systemic contamination and in a small increase in the concentration of uranium in the urine. The figures are not amenable to exact interpretation. It appears, however, that six months after the accident the uranium-in-urine figures had returned to pre-accident levels.

Ashing and analysis of postmortem tissues

Before analysis it was necessary to dry and ash the

TABLE 3
CONCENTRATIONS OF URANIUM IN END-OF-SHIFT URINE SAMPLES

<i>Year</i>	<i>Quarter</i>	<i>No. of samples</i>	<i>Uranium concentration (μg/l) (range)</i>	<i>Year</i>	<i>Quarter</i>	<i>No. of samples</i>	<i>Uranium concentration (μg/l) (range)</i>
1959	1	7	0-10	1965	1	0	—
	2	7	0-20		2	2	0-10
	3	6	0-40		3	3	0-40
	4	3	0-40		4	4	0-10
1960	1	4	0-10	1966	1	3	0-40
	2	1	5		2	3	0-5
	3	1	5-10		3	1	0-5
	4	2	5-20		4	2	0-10
1961	1	2	5-10	1967	1	3	0-10
	2	2	0-10		2	2	0-5
	3	2	0-10		3	3	0-40
	4	1	5-10		4	2	0-20
1962	1	3	0-10	1968	1	5	0-40
	2	3	5-20		2	25	0-80
	3	4	0-20		3	28	10-100
	4	5	0-60		4	9	10-80
1963	1	3	5-20	1969	1	4	5-40
	2	0	—		2	1	0-5
	3	4	0-10		3	2	0-20
	4	4	0-20				
1964	1	2	0-5				
	2	3	0-10				
	3	2	0-10				
	4	4	0-10				

samples to convert them to a suitable size. The deep-frozen tissue samples were cut into approximately 2-cm cubes, taking precautions to avoid contamination¹, and dried for at least 48 hours in vacuum desiccators. The sternum was cut into small pieces with a hacksaw and similarly dried.

The delayed neutron method of uranium determination was chosen and used by one of us (J.S.H.) because it is simple, sensitive, non-destructive, and less susceptible to problems of reagent contamination¹ than conventional chemical methods. The technique consists basically of irradiation of the sample in a thermal neutron flux and comparison of the delayed neutron activity, produced from such uranium fission products as ⁸⁷Br, with that produced from a uranium standard. The technique has been widely used for the determination of U in a number of matrices (Amiel, 1961; Dyer, Emery, and Leddicotte, 1962; Gale, 1967). Some details of the procedure used are given in the Appendix.

¹Uranium is an important constituent of about 100 mineral species; it is present in air and water in measurable quantities. In the analytical laboratory uranium is therefore regarded as an ubiquitous trace element, and reagents are assumed to contain uranium until it has been proved that they do not.

The results of the analyses are given in Table 4, and in Table 5 an attempt is made to estimate the distribution of uranium in different organs.

Discussion

Lungs

At the New York Symposium one of the main items reported and discussed concerned the unexpectedly low retention of insoluble uranium in the human lung. Eisenbud (1958) remarked that whereas the low lung retention figures were curious and reassuring they required explanation. His own view was that the high density of the dust was responsible for the low alveolar deposition rate. Uranium oxides have a density of 9 or 10 g/ml, and because of this—Eisenbud suggested—two-micron particles may not reach the alveoli at all. The continuation of this discussion since 1958 has been limited by the paucity of data, especially human data. This is evident from the sketchiness of the investigations summarized in Tables 1 and 6. As far as the present investigation is concerned, it is clear that the low lung retention figures fit in well with those reported by Quigley and his colleagues (1958), by Butterworth (1958), and by Meichen (1962). Whether or

TABLE 4
WET WEIGHTS, ASHED WEIGHTS, AND NATURAL URANIUM CONTENT OF POSTMORTEM TISSUES

Tissue	Wet wt. (g)	Ashed wt. ¹ (g)	Uranium content ² (μg)	Ashing procedure before analysis ³
Left upper lung	254	2.63	355.6	20 h at 500°C
Left lower lung	252	2.52	278.6	20 h at 500°C
Right upper lung	218	2.24	263.3	20 h at 500°C
Right lower lung	254	2.56	263.8	20 h at 500°C
Right middle lung	72	0.80	87.3	80 h at 100°C in active O ₂
Left lymph node	5.0	0.08	9.6	Dried only
Right lymph node	7.0	0.11	12.3	Dried only
Liver	177	1.97	3.8	20 h at 500°C
Kidney (medulla)	56	0.60	5.3	80 h at 100°C in active O ₂
Kidney (cortex)	161	1.56	26.2	20 h at 500°C
Sternum	114	16.7	10.1	20 h at 550°C

¹Ashing to constant weight (by ignition at 500°C) carried out after analysis for uranium.

²Analysis is based on measurement of ²³⁵U and the weight of uranium quoted assumes ²³⁵U is present in natural abundance.

³It was shown that the most severe ashing procedure used before uranium determination (20 h at 500°C) did not result in loss of uranium from either lung tissue or kidney tissue.

not we accept the assumptions customarily used to estimate uranium lung burdens from air contamination data, a chest burden of 1.3 mg following a long exposure to 300 μg/m³ (2.5 mg/day) is significantly small (see Table 5).

Lymph nodes

The low level of uranium in the lymph nodes appears to be entirely consistent with earlier human data. As far as we can ascertain, the concern about the vulnerability of the lymph nodes began with the

TABLE 5
DISTRIBUTION OF URANIUM IN POSTMORTEM TISSUES

Tissue	Wet weight (g)	Uranium concentrations (μg U/g wet weight)	Weight in tissues (μg)	(Likely) weight in whole organ (μg)
Lung lobes				
Left upper ..	254	1.4	355.6	1250
Left lower ..	252	1.1	278.6	
Right upper ..	218	1.2	263.3	
Right lower ..	245	1.1	263.8	
Right middle	72	1.2	87.3	
Lymph nodes				
Left	5.0	1.9	9.6	35 ¹
Right	7.0	1.8	12.3	
Sternum	114	0.09	10.1	1000 ²
Kidney				
Cortex	161	0.16	26.2	30
Medulla	56	0.09	5.3	
Liver	177	0.02	3.8	35
Blood		(0.01) ³	—	(50)

¹In the tracheobronchial lymph nodes

²In the entire skeleton (assuming a skeletal weight of 10 kg and a uniform distribution of uranium in the skeleton)

³A conjectural figure, precariously based on data provided by Hamilton whose investigations on tissues from unexposed humans in the U.K. show that the concentration of uranium in blood is 0.84 ng U/g wet weight. The equivalent amount in total blood is 4.5 μg. See *Nature (Lond.)*, 227, pp. 501-502, Aug. 1, 1970.

TABLE 6
DEPOSITED URANIUM IN UNEXPOSED AND EXPOSED HUMAN SUBJECTS

Investigator and case	Year	Exposure	Concentration of uranium ($\mu\text{g U/g wet tissue}$)			
			Lung	Kidney	Bone	Liver
Quigley <i>et al.</i> V ¹ ..	1958	None	0.089	0.026	0.028	0.093
Quigley <i>et al.</i> V1 ¹ ..	1958	None	0.006	0.020	0.004	0.008
Butterworth, C.1 ..	1958	None	0.05	—	—	0.02
Lynch, I ..	1966	None	—	0.03	—	—
Hamilton ..	1969	None	—	—	0.004	—
Butterworth, D.46 ..	1958	Soluble	0.15	0.08	—	—
Butterworth, D.99 ..	1958	Insoluble	0.05 ^a	0.06	—	—
Quigley <i>et al.</i> , III ¹ ..	1958	Insoluble	1.02	0.038	0.048	—
Meichen, 7 ..	1962	Unknown	1.6	0.12	—	0.04
Donoghue <i>et al.</i> ..	1970	Insoluble	1.2	0.14	0.09	0.02

¹Quigley stressed the advisability of analysing fresh postmortem tissue which has not been placed in a chemical preservative. Some of his data, however, were obtained from preserved tissues and on this account may be less reliable.

^aThe concentration of uranium in the associated lymph nodes was 0.12 $\mu\text{g/g wet tissue}$.

Manhattan Project; it was raised by Hodge and Thomas at the Geneva Conference in 1958 (if not before) and was for some years regarded as a potential radiological bogey. As far as natural uranium is concerned there was little justification for this.

In the dog experiments reported by Hodge and Thomas (1959), in which UO_2 was used, the concentration of uranium in the lymph nodes was admittedly high (1.5–29.0 mg U/g wet tissue) and between 1.4 and 13.2 times the concentration in the lungs. The exposure level was, however, also high (5 mg/m³). This information was confirmed and extended in a recent report by Leach and his colleagues (1970) of a more thorough investigation in which monkeys, dogs, and rats inhaled natural UO_2 dust of 1 $\mu\text{m MMD}$, at a concentration of 5 mg U/m³, six hours per day, five days per week for periods up to five years. In this investigation the concentration of uranium ($\mu\text{g U/g fresh tissue}$) in the lymph nodes of dogs exposed for five years was roughly 50, and in the lungs roughly 1.8. Under these conditions this ratio (concentration in lymph nodes divided by concentration in lungs) increased from about 3 after one year's exposure to about 8 after two years and about 20 after five years. It seems that a sufficiently high atmospheric concentration of finely divided dust leads inevitably to a clogging of the normal physiological pathways, and this kind of partial suffocation is probably a different process (though not always distinguishable) from toxic action. The fact that at high atmospheric concentrations UO_2 accumulates more rapidly ($\mu\text{g/g}$) in the lymph nodes than it does in the lungs is not a reliable indication that the same phenomenon will occur at lower concentrations; it may, or it may not,

depending on the atmospheric concentration, the length of exposure, the animal, and the dust. Some results, however, were obtained on animals exposed to lower levels. The dogs used in Fish's experiments were exposed to a U_3O_8 aerosol at a concentration of 500 $\mu\text{g/m}^3$ for short periods which limited the inhaled dose to 25 $\mu\text{g/week}$. After six months the concentration of uranium in the lungs was 25 $\mu\text{g/g wet tissue}$. The concentration in the lymph nodes was 15 $\mu\text{g/g wet tissue}$ and seemed likely eventually to exceed the concentration in the lungs. On the basis of these figures, Fish (1961) tentatively suggested that the MPC for insoluble uranium 'be reduced by a factor of about 30'. The value of these findings from animals is partly outweighed by human occupational figures, which have so far been consistently low. In Meichen's case 7 (Table 6), for example, the concentration of uranium in the lymph nodes was 0.32 and in the lungs 1.6 $\mu\text{g/g wet tissue}$ (Meichen, 1962).

Nasopharynx

A large proportion of the inhaled dust is deposited in the nasopharynx, of which—according to the model proposed by the I.C.R.P. Task Group—99% is transported to the gastrointestinal tract and 1% to the blood. It is conceivable, however, that some of the dust deposited in the nasopharynx is transported to and retained in the air sinuses of the skull. If this is regarded as a likely possibility, consideration should be given to the feasibility of monitoring the head as well as the chest in uranium retention investigations.

Bone

According to Hamilton (1969), who has recently

made estimates of uranium in bone from persons with no occupational exposure, the average figure in the U.K. is $0.024 \mu\text{g U/g}$ ash for the skeleton as a whole and $0.018 \mu\text{g/g}$ for the sternum. The figure given by Welford and Baird (1967—Table 4) for the concentration of uranium in 'unexposed' human bone in the U.S.A. is closely similar— $0.020 \mu\text{g/g}$ ash. (It is unfortunate that in the text of this paper and in a recent abstract (International Atomic Energy Agency, 1970) this figure is misleadingly given as $0.2 \mu\text{g/g}$ ash.) Taking the figure for the sternum from Table 4 ($0.6 \mu\text{g/g}$ ash) and comparing it with Hamilton's result, gives an exposed/unexposed ratio of, in this case, about 30.

Kidneys

At dissection the cortex, which contains more of the glomeruli and the convoluted tubules, was separated from the medulla, which contains the collecting tubules. The fact that the ratio of the uranium-in-kidney concentrations, cortex/medulla, is significantly greater than one, agrees with the result of Hamilton's animal experiments. It is also supported by the autoradiograph shown as their Fig. 8 by Bernard and Struxness (1957).

Relevance to I.C.R.P. recommendations

According to the International Commission on Radiological Protection (1960), the fractional distribution of uranium relative to that in the whole body is 0.85 in bone and 0.065 in kidneys. If we use the results from Table 5, including the conjectural figure for blood and excluding the figure for the lungs (which are metabolically outside the body), the corresponding figures are 0.87 and 0.026.

Using the model offered by the I.C.R.P. Task Group in 1966 and the exposure data, we may estimate the amount of uranium deposited each day provided we have a figure for the amount of air breathed during the working day. From published information about the relationship between inhalation rate and degree of physical exertion (Hatch and Gross, 1964; International Commission on Radiological Protection, 1966) and from knowledge of this worker's occupational history, it was estimated that the volume of air breathed during each working shift was about 8 m^3 . On this basis the daily deposition of uranium in the nasopharynx was about 2.15 mg , in the pulmonary compartment about 0.6 mg , and in the tracheobronchial compartment about 0.25 mg . Absorption from each of these sites contributed to a urinary excretion rate of between 5 and $30 \mu\text{g}$ uranium per day.

The weights of uranium found in the lungs and lymph nodes are much smaller than the amounts predicted by the I.C.R.P. lung model, which employs a series of single exponential compartments. Insoluble uranium falls in the category of materials

whose rate of removal from the pulmonary compartment (lung) and lymph nodes is assumed by the I.C.R.P. to have a 360-day half-life. Exposure to airborne dust of A.M.A.D. $5 \mu\text{m}$ at a concentration of $300 \mu\text{g/m}^3$ would be expected to result in an equilibrium retention of 190 mg in the lungs and 160 mg in the lymph nodes. For the lung the measured amount is 0.7% of that calculated and for the lymph nodes 0.02% .

In commenting on these reassuringly low figures we may resort to either of the following interpretations. On the one hand, it is possible but unlikely that the rate of deposition of uranium oxides in the lungs is more or less identical with that calculated on the basis of the I.C.R.P. assumptions (i.e., 0.6 mg/day). The exponential clearance model would then require the biological half-life of the dust in the lungs to be not 360 days, but 2 days. The feasibility of this interpretation is not supported either by the relatively low solubility of U_3O_8 (see, for example, Steckel and West (1966)) or by the evidence of Schultz (1966) and Ronen (1969) concerning the long biological half-life of retained U_3O_8 . On the other hand, it is possible and perhaps less unlikely, that the rate of deposition of uranium oxides in the pulmonary compartment is smaller than that calculated on the basis of I.C.R.P. assumptions; in this case the 360-day biological half-life could be regarded as consistent with the measured amount of uranium in the lungs. Evidence to support this assumption is provided by the low concentrations of uranium in urine. Each of these interpretations would require modification if the airborne uranium oxide, which has a small but significant solubility in blood, contained a proportion of a uranium compound of negligible solubility and transportability.

Conclusions

A postmortem study is presented in which the amounts of natural uranium found in the lungs and lymph nodes are much smaller than those predicted by calculations using exposure data and the current lung model. Any discussion concerning the fate of inhaled 'insoluble' uranium must, therefore, allow for at least two kinds of evidence—that indicating a low deposition in the lung, as in the present case, and that indicating a high deposition. Both are illustrated in Table 1. The explanation of this apparent anomaly lies partly in physiological idiosyncrasy and partly in the ambiguity of phrases like 'insoluble uranium' and 'uranium oxide'. Committee II of the I.C.R.P. explained 12 years ago that the 'retention of particulate matter in the lungs depends on many factors, such as the size, shape and density of the particles, the chemical form and whether or not the person is a mouth breather'. In investigations

into the health hazards from natural uranium the quantities of the contaminant are sufficiently large to permit thorough physical and chemical examinations. It may be that the explanation of some present anomalies awaits the availability of case histories with more detailed information of the physical and chemical properties of the aerosol, and, where appropriate, of physiological idiosyncrasy.

Appendix

Some details of the ashing procedure and the analytical method

Several investigators have shown that dry ashing may give rise to loss of volatile species of certain elements (Hamilton, Minski, and Cleary, 1967). Little or no information is available, however, on the behaviour of uranium. As it was considered that both metabolized (e.g., in kidney) and non-metabolized (e.g., in lung) uranium might be present, a preliminary investigation was carried out to determine whether dry ashing procedures resulted in loss of uranium from both types of tissue. Both lymph nodes and a portion of the kidney were sufficiently small, after drying, to enable them to be packed in polyethylene irradiation containers and analysed without ashing. After analysis these samples were ashed in silica basins at 500°C for approximately 20 hours and the uranium content was redetermined. In both types of tissue it was found that no significant loss of uranium occurred during this ashing procedure. Consequently, the majority of samples were ashed in silica at 500°C for approximately 20 hours. During the investigation of ashing technique for this type of material an attempt was made to ash the right middle lung and the kidney medulla in a Tracerlab LTA 600 low-temperature asher. It was possible to reduce the bulk sufficiently for analysis but because of the slowness of the ashing procedure this was not a satisfactory technique for this type of material. No attempt was made to ash to constant weight before analysis, but all samples were ashed to constant weight after analysis to enable the results to be expressed as $\mu\text{g U/g ash}$ in addition to $\mu\text{g U/g wet tissue}$.

Samples were packed in heat-sealed 7-ml polyethylene containers and were irradiated for 1 minute in a neutron flux (1.5×10^{13} n/cm²/s thermal, 5×10^9 n/cm²/s fast) using the rapid rabbit facility in the 12 HGR-2 core location of DIDO at Harwell. A 25-second delay was incorporated after irradiation to enable removal of the outer rabbit container and to minimize interference from neutrons produced from ¹⁷N. The samples were then counted for 1 minute using a series of eight BF₃ counters and associated Harwell 2000 series electronics, as described by Gale (1967). Standards containing weights of natural uranium comparable to those in the samples were prepared by evaporating weighed

aliquots of uranium nitrate solution on 4×5 cm sheets of polythene and these were irradiated and counted similarly to the samples.

The background of the counting equipment, including the activity from the uranium content of empty polyethylene containers, was 250 counts per minute. The specific activity obtained was 1 000 ct/min/ μg natural uranium. The precision of each determination on the basis of counting statistics was better than $\pm 2\%$ (1σ) but it was found that the overall precision of the method was 2 to 3% (1σ). The neutron counters were shielded from the samples by 3.75 cm lead and with this shield in position the gamma-ray activity of the irradiated samples was shown to be insufficient to cause false neutron counts due to electronic pulse pile up.

Delayed neutrons may be obtained from sources other than fission of uranium, e.g., from fission of plutonium and thorium. The possibility of plutonium contamination was considered to be negligible. Because the method used is relatively insensitive to thorium, contamination with thorium was also regarded as negligible. As the fission of ²³⁵U is used for measurement, the isotopic composition of the uranium to which the subject has been exposed is significant. The results given in Table 4 are based on the assumption (which in this investigation is known to be justified) that uranium is present in natural isotopic abundance.

The authors are indebted to Dr. E. I. Hamilton of the Radiological Protection Service, Sutton, Surrey for helpful comments on the draft of this paper and for access to unpublished information. They are grateful to Mr. A. B. Crowther, U.K.A.E.A. (Production Group), for arranging the analysis of the settled dust from the workshop, and to Mr. A. D. Pratchett, U.K.A.E.A. (Research Group), for assisting in the analysis of the postmortem tissues.

References

- Amiel, S. (1961). Analytical applications of delayed neutron emission in fissionable elements. Israel Atomic Energy Commission Report IA-621.
- Bernard, S. R., and Struxness, E. G. (1957). A study of the distribution and excretion of uranium in man. USAEC Report ORNL-2304.
- Butterworth, A. (1958). Human data on uranium exposure. In: *Symposium on Occupational Health Experience and Practices in the Uranium Industry, New York 1958*, pp. 41-46. USAEC Report HASL-58.
- Butterworth, R., and Donoghue, J. K. (1970). Contribution of activity released from protective clothing to air contamination measured by personal air samplers. *Health Phys.*, **18**, 319-323.
- Dyer, F. F., Emery, J. F., and Leddicotte, G. W. (1962). A Comprehensive Study of the Neutron Activation Analysis of Uranium by Delayed-Neutron Counting. USAEC Report ORNL-3342.
- Eisenbud, M. (1958). Discussion of apparent anomalies in lung retention of uranium. In: *Symposium on Occupational Health Experience and Practices in the Uranium Industry*, pp. 212-213. USAEC Report HASL-58.

- Fish, B. R. (1961). Inhalation of uranium aerosols by mouse, rat, dog and man. In: *Inhaled Particles and Vapours*, edited by C. N. Davies, pp. 151. Pergamon Press, Oxford.
- , and Patterson, G. R. (1958). Report WASH-1023 (TID 4500).
- Gale, N. H. (1967). Development of delayed neutron technique as rapid and precise method for determination of uranium and thorium at trace levels in rocks and minerals, with applications to isotope geochronology. In: *Radioactive Dating and Methods of Low-Level Counting*, pp. 431-452. IAEA, Vienna.
- Hamilton, E. I. (1969). Personal communication.
- , Minski, M. J., and Cleary, J. J. (1967). The loss of elements during the decomposition of biological materials with special reference to arsenic, sodium, strontium, and zinc. *Analyst*, **92**, 257-259.
- Hatch, T. F., and Gross, P. (1964). *Pulmonary Deposition and Retention of Inhaled Aerosols*. Academic Press, New York.
- Hodge, H. C., and Thomas, R. G. (1959). The questions of health hazards from the inhalation of insoluble uranium and thorium oxides. In: *Progress in Nuclear Energy, Series XII, Health Physics*, vol. 1, ed. W. G. Marley and K. Z. Morgan, pp. 52-59. Pergamon Press, London.
- International Atomic Energy Agency (1970). Detection and assessment of uranium and plutonium in the whole body and in the critical organs. Report IAEA-118.
- International Commission on Radiological Protection (1960). Report of Committee II on Permissible Dose for Internal Radiation (1959). Pergamon Press, Oxford. *Hlth Phys.*, **3**, 1-233.
- International Commission on Radiological Protection, Task Group on Lung Dynamics (1966). Deposition and retention models for internal dosimetry of the human respiratory tract. *Hlth Phys.*, **12**, 173-207.
- Leach, L. J., Maynard, E. A., Hodge, H. C., Scott, J. K., Yuile, C. L., Sylvester, G. E., and Wilson, H. B. (1970). A five-year inhalation study with natural uranium dioxide (UO₂) dust—I. Retention and biologic effect in the monkey, dog and rat. *Hlth Phys.*, **18**, 599-612.
- Lynch, J. B. (1966). Personal communication.
- McLendon, J. D. (1959). Report AECU 4089.
- Meichen, F. W. (1962). Medical supervision of employees in the atomic energy industry. *Atompraxis*, **8**, 24-26.
- Miller, C. E. (1957, 1958). Semi-annual Progress Reports ANL 5829 and ANL 5919.
- Quastel, M. R., Taniguchi, H., Overton, T. R., and Abbatt, J. D. (1970). Excretion and retention by humans of chronically inhaled uranium dioxide. *Hlth Phys.*, **18**, 233-244.
- Quigley, J. A., Heatherton, R. C., and Ziegler, J. F. (1958). Studies of human exposure to uranium. In: *Symposium on Occupational Health Experience and Practices in the Uranium Industry*, pp. 34-40. USAEC Report HASL-58.
- Ronen, M. (1969). A case of insoluble natural-uranium exposure: a two-year follow-up study. In: *Proceedings of Symposium on the Handling of Radiation Accidents*. IAEA, Vienna.
- Saxby, W. N., Taylor, N. A., Garland, J., Rundo, J., and Newton, D. (1964). A case of inhalation of enriched uranium dust. In: *Assessment of Radioactivity in Man*, vol. II, pp. 535-547. IAEA, Vienna.
- Schultz, N. B. (1966). Report K-C-822 (IRPA Congress, Rome).
- Scott, L. M., and West, C. M. (1964). Detection and evaluation of uranium exposures. In: *Assessment of Radioactivity in Man*, vol. II, pp. 523-533. IAEA, Vienna.
- Sherwood, R. J., and Greenhalgh, D. M. S. (1960). A personal air sampler. *Ann. occup. Hyg.*, **2**, 127-132.
- Steckel, L. M., and West, C. M. (1966). Characterization of Y-12 uranium process materials correlated with in vivo experience. Union Carbide Corporation, Nuclear Division, Report Y-1544-A.
- Welford, G. A., and Baird, R. (1967). Uranium levels in human diet and biological materials. *Hlth Phys.*, **13**, 1321-1324.
- West, C. M., and Scott, L. M. (1969). Uranium cases showing long chest burden retention—an updating. *Hlth Phys.*, **17**, 781-791.

Received for publication March 17, 1971