Incorporation of Uranium

I. Distribution of Intravenously and Intraperitoneally Injected Uranium

G. WALINDER¹, L. HAMMARSTRÖM and U. BILLAUDELLE

From AB Atomenergi, Stockholm 43, and the Royal Veterinary College, Stockholm 50, Sweden

The distribution of uranium in mice following intravenous and intraperitoneal injections of uranyl nitrate and uranyl tricarbonate was studied by autoradiographic and fluorometric methods at different times after administration. The investigations revealed a higher retention of uranium in the spleen and bone than in other organs, including the kidneys.

We have been able to show that even very small amounts of uranium give rise to ischaemia in the kidney. A higher initial uptake was found in the juxtamedullary zone than in the more peripheral parts of the renal cortex. The retention, however, was higher in the peripheral cortex. This may explain the fact that the first observable damage in the kidney appears in the juxtamedullary zone. The connexion between blood supply and uranium uptake and retention in different zones of the renal cortex is discussed with special regard to the toxicological consequences of uranium incorporation and to the possibility of accelerating the excretion of uranium.

The present investigations were designed to examine the extent to which the distribution of uranium in mammalian organisms is dependent on the mode of administration. The findings will be reported in two papers. Part I, which is presented here, contains autoradiographic and quantitative studies of the uranium distribution in mice following intravenous and intraperitoneal injections of uranyl nitrate and uranyl tricarbonate. In addition, two piglets were used for fluorometric determination of the uranium content of some organs after injection of uranyl tricarbonate into an ear vein. Part II (p. 313, this journal) is concerned with the corresponding distribution pattern following the inhalation of U_3O_8 aerosol in mice, and absorption of uranyl acetate through skin incisions in rabbits and pigs. In some experiments on the two last-named species chemical agents were used to try to prevent the penetration of uranium through the skin.

For an appraisal of the risks associated with the handling of uranium, the distribution pattern observed after direct intravenous injections will be of little help unless it can be shown that the relative amounts taken up by the organs do not depend on the mode of entry of uranium into the organism.

Uranium incorporated from depots in the lungs and skin always combines, in the body fluids, with proteins (40%) and with bicarbonate in the form of complex anions (Hodge, 1956; Dounce, 1949). If there is an excess of bicarbonate ions it is principally uranyl tricarbonate $UO_2(CO_3)_3^{4-}$ that will be formed (Galkin, Maiorov, and Veryatin, 1963). Absorption from depots in the body is not direct; the uranium, if not already in hexavalent form, first undergoes oxidation and is then complexed with protein and carbonate ions. When carbonate-bound uranium is excreted by the kidneys, a shift takes place in the blood, whereby the ratio of protein-bound to carbonate-bound uranium is maintained. Apparently there is no appreciable tendency towards agglomeration or precipitation in the blood since the uranium disappears rapidly from the blood stream and is taken up, notably by the bones and kidneys, but not on any major scale by the liver; it also appears in the urine. Forty minutes after an intravenous injection, not more than about 1% remains in the blood (Hodge, 1956). When uranyl nitrate is injected intravenously, anion formation occurs very swiftly, for no qualitative or quantitative difference can be detected in mice following injection of uranyl nitrate and of uranyl tricarbonate respectively (Table I). To avoid side effects from the slightly acid uranyl nitrate solutions we have

¹Present address: Research Institute of National Defence, Dept. 1, Sundbyberg 4, Sweden.

Received for publication June 1, 1967.

TABLE I

URANIUM CONCENTRATIONS IN ORGANS OF MICE FOLLOWING INTRAPERITONEAL INJECTION EQUIVALENT TO 30 µg. NATURAL URANIUM

Days after Injection	Uranium Compound Injected	Liver (µg./g.)	Spleen (µg./g.)	Kidneys (µg./g.)	Sternum (µg./g.)	Tibia (µg./g.)	Urine (µg./animal)	Faeces (µg./animal)	Remarks
1	Nitrate	0.21	1.8	18.0	3.8	1.9	16.0	0.20	
	"	0.43	1.7	14.9	3.6	2.6			
	"	0.60	1.7	14.2	1.8	1.2	14.0	0.55	
	"	0.57	1.9	16.8	1.4	1.2			
	Tricarbonate	0.22	3.8	15.7	2.1	2.7	19.0	—	
	"	0.22	3.3	21.2	4.2	2.2			
	"	0.31	1.8	18.6	3.1	2.0	8.0	0.40	
	"	0.33	1.7	20.6	4.2	2.0			
	"	0.70	2.4	13.6	3.3	—	12.0	—	
2	"	0.70	2.4	13.2	—	—			
	Nitrate						1.9	—	
	"						—	0.12	
	"						1.7	0.11	
	Tricarbonate						0.8	0.12	
3	"						1.8	0.10	
	"						1.7	—	
	Nitrate						0.75	0.222	
	"						0.96	0.051	
	Tricarbonate						0.85	—	
7	"						0.80	—	
	"						0.70	—	
	Nitrate	0.068	0.91	7.2	0.73	0.66	0.084	0.090	
	"	0.039	0.75	4.8	0.96	0.62			
	"	0.087	1.4	—	0.91	0.68	0.16	0.052	
	Tricarbonate	0.044	0.51	4.0	0.71	0.62	0.072	0.054	
	"	0.044	1.3	6.7	1.1	0.62			
	"	0.066	0.64	5.2	0.91	0.54	0.14	0.12	
	"	0.065	0.56	4.8	0.75	0.65			
14	"	0.076	1.0	4.0	1.2	1.0	—	—	
	"	0.050	0.45	3.9	1.2	—			
	Nitrate	0.027	0.22	0.79	0.21	0.20	0.012	0.018	
	"	0.023	0.26	0.67	0.36	0.30			
	"	0.023	0.20	0.98	0.29	0.32	0.022	0.023	
	"	0.027	0.42	1.1	0.25	0.21			
	Tricarbonate	0.025	0.20	1.5	0.52	0.31	0.017	0.036	
	"	0.036	0.38	1.3	0.50	—			
	"	0.022	0.31	—	0.66	0.43	0.036	0.021	
30	"	0.028	0.42	—	0.45	0.47			
	Nitrate	0.019	0.20	0.26	0.28	0.15	0.008	0.018	
	"	0.022	0.16	0.34	0.32	0.28			
	"	0.024	0.23	0.16	0.29	0.23	0.007	0.012	
	"	0.020	0.20	0.20	0.37	0.20			
	Tricarbonate	0.032	0.24	0.28	0.43	0.27	0.008	0.013	
	"	0.020	0.24	0.29	0.56	0.31			
	"	0.020	0.26	0.40	0.37	0.48	0.012	0.011	
	"	0.024	0.41	0.30	0.45	0.36			
60	"	0.020	0.40	0.28	0.57	0.46	0.007	—	
	Tricarbonate	0.027	0.10	0.23	0.42	0.42			Organs from two mice combined
	"	0.028	0.13	0.23	0.35	0.38			
76	"	0.018	0.17	0.10	0.41	0.24			
	Nitrate	0.019	0.07	0.10	0.35				Organs from three mice combined
217	Tricarbonate	0.0015 ¹	0.010	0.0010 ¹	0.043	0.052			Organs from five mice combined

¹Background values.

preferred to inject neutral uranyl tricarbonate solutions.

Autoradiographic Investigations

Uranyl tricarbonate was prepared by dissolving the nitrate in a solution containing 0.7% NaCl and 0.22% NaHCO_3 (26 mM NaHCO_3), i.e., an HCO_3^- concentration equal to that in normal blood; 300 μg . of natural uranium and 210 μg . ^{233}U was dissolved as uranyl nitrate in 1 ml. of these solutions. Because of the excess of HCO_3^- ions the uranium is combined with bicarbonate, entirely in the form of uranyl tricarbonate (Galkin *et al.*, 1963). In experimental dialysis with carbonate-bound uranium and uranyl nitrate in blood, we found identical diffusion curves.

Whole-body Autoradiography The nuclide ^{233}U as sodium uranyl tricarbonate was injected into a tail vein in mice. This dose contained 42 μg . uranium (0.2 ml.), the equivalent of 0.4 μCi .

Seven C-57 leaden mice, four adult males and three adult females, were used for whole-body autoradiography. The intervals between injection and killing were 24 hours, nine days, 30 days, and six months respectively for the males, and 24 hours, nine days, and 30 days respectively for the females. Following anaesthetization with ether the animals were killed by immersion in hexane chilled to -75°C . with solid carbon dioxide. Whole-body sagittal sections, 20 μ thick, were taken at various levels at -10°C . and dried at the same temperature. The sections were then pressed against Structurix (Gevaert) X-ray film. The exposure time was two to six months. Details of the autoradiographic method have been reported by Ullberg (1954).

Microautoradiography Uranium was injected as in whole-body autoradiography. After varying intervals the animals were killed and the kidneys and spleens were removed, fixed in neutral formalin, dehydrated, embedded in paraffin, and then sliced into sections 5 μ thick. The slices were covered with stripping film (AR 10, Kodak) in accordance with the method of Doniach and Pelc (1950). Following exposure and development of the film the sections were stained with haematoxylin and eosin, dried in alcohol, and mounted in Canada balsam under cover glasses.

Results (Figs 1—3) After 24 hours the concentration of uranium in the blood was low. Accumulations of the isotope were noted in the kidneys, liver, spleen, adrenal cortex, bones, and teeth.

Although the concentrations gradually decreased, radioactivity was still detectable six months after the injection. Of the uptake by soft tissues, that in the spleen seemed to persist the longest.

The highest uranium concentration 24 hours after the injection was found in the renal cortex, particularly in the inner part. However, the concentration fell more rapidly in the inner than in the outer cortical zone. At 30 days the kidneys showed accumulation of radioactivity in a narrow peripheral zone, and at six months only very slight activity remained, with no detectable local accumulation.

The liver was found to have a lower concentration than the renal cortex. Moreover, the radioactivity was not evenly distributed but scattered among numerous discrete areas. The uptake was relatively high at 24 hours, but the concentration then fell rapidly. This initially high uptake could not, however, be verified by quantitative uranium determination in liver tissue.

Radioactivity persisted longer in the spleen than in other soft tissue. The uptake was localized principally in the marginal sinuses. On micro-autoradiographs of a mouse spleen six months after the injection the uranium was extracellular, in cell debris.

The adrenal cortex had a moderate uptake which was still detectable six months after the injection.

In bone, the uranium was localized in the endosteum and periosteum; and in the teeth it was taken up by newly formed enamel and dentin.

Quantitative Investigations

All the mice used in these experiments were males (CBA), approximately 3 months old. The injections were intraperitoneal, except in a few mice in which the solution was injected into a tail vein in order to find out if the distribution patterns were different between the intraperitoneal and intravenous rates of administration.

In addition to the above, uranyl tricarbonate was injected into an ear vein of two piglets, 3 months old, weighing 23 and 25 kg.

The uranium content of various organs was determined fluorometrically.

Materials and Methods The fluorometric method used in this study permits determinations down to a lower limit of 0.002 μg . Since organic and inorganic compounds affect the fluorescence in a way that is not yet fully understood, it is essential to remove all impurities from the uranium. In the

FIG. 1. Autoradiographs of sagittal whole-body sections of mice killed at different times after intravenous injection of ^{233}U as sodium uranyl tricarbonate.

A. Distribution of uranium one day after the injection. Note the high concentrations at the cortico-medullary junction of the kidney and the marginal sinuses of the spleen.

B. Distribution after nine days. The activity now appears to be more evenly distributed in the cortex of the kidney. The concentration is substantially lower in the liver than in the spleen and the renal cortex.

C. Distribution after 30 days. In the kidney, uranium is localized within a narrow zone of the outer cortex.

D. Distribution after six months. The little activity which persists in the kidney is homogeneously distributed. Retention appears to be greater in the spleen than in other soft tissues.

FIG. 2. Autoradiograph showing the uranium distribution in a pelvic bone one day after the injection. The radioactivity is substantially localized in the periosteum, endosteum, and bone trabeculae.

FIG. 3. Detail from autoradiograph showing accumulation of uranium in the adrenal cortex one day after intravenous injection. Radioactivity was still detectable in the adrenal cortex six months after the injection.

present investigation this was done by serial boiling in different oxidizing acids.

The organic tissue was boiled in concentrated HNO_3 and H_2SO_4 under reflux until the original golden brown colour of the solution changed to light green. No evaporation could be undertaken until this change had occurred or it would immediately have led to total or partial charring. If carbonization starts, it greatly hinders digestion.

Concentration then followed, after addition of HClO_4 . The solid residue of inorganic salts was dissolved in a little HNO_3 . After the addition of a saturated $\text{Al}(\text{NO}_3)_3$ solution, the inorganic uranyl salts were removed by extraction with ethyl acetate. The end product thus obtained was sufficiently pure to cause no disturbances of fluorescence at the subsequent measuring procedure. (In the hands of an experienced laboratory assistant the method shows a yield in excess of 95%.) When the organ studied had a low uranium content it was necessary to concentrate the ethyl acetate solution. In such cases, the yield was less satisfactory and could fall to around 80%, probably due largely to adherence to the walls of the evaporation vessel.

At the lower limit of this fluorometric method (0.002 $\mu\text{g.}$) the accuracy of measurement is, of course, low. For uranium quantities exceeding 0.01 $\mu\text{g.}$, however, the variation on measurement of standard specimens was found to be negligible by comparison with the variations caused by biological factors and losses associated with digestion of the biological material. As a rule two animals were examined simultaneously and the yield was controlled by a parallel analysis of a spiked liver sample.

The quantity injected was always 30 $\mu\text{g.}$ uranium per mouse and 180 $\mu\text{g.}$ per pig.

Results In Table I the uranium concentration in the various organs is recorded so that each row of figures refers to a single animal. Some idea of the total uptakes can be gained from the mean weights of particular organs which are listed below. Due to the homogeneity of the experimental material there was very little variation in organ weights, which were: liver, 1.62 g.; spleen, 77 mg.; kidneys, 0.47 g.; skeleton, 1.35 g. (Tannenbaum, Silverstone, and Koziol, 1951). Urine specimens were taken from five mice which were kept for 24 hours in a cage specially designed for quantitative collection of urine.

Twenty-four hours after the injection the highest uranium concentration was in the kidneys and exceeded the concentrations in the spleen and bone by factors of 5 to 10. The corresponding values

for liver were considerably lower than is suggested by the autoradiographs. Radiometric determinations of the uranium content of each organ following intravenous injection of ^{233}U in CBA mice gave the same results as the fluorometric analyses. The discrepant liver uptakes may, of course, be attributable to differences between the C-57 leaven and the CBA mouse. We did not investigate this question.

The uranium content fell more rapidly in the kidneys than in the bone and spleen, so that after one or two months the concentrations were approximately equal in the three tissues. At six months, bone and spleen contained higher concentrations than did the kidneys. (Concentrations are averages as the concentration is not uniform throughout a given tissue.)

As a rule, organs from two animals were analysed concurrently under virtually identical conditions. Hence, the variability is consistently smaller for intra-group than for inter-group values.

The natural uranium content of various organs was determined in untreated mice, for which purpose the corresponding organs from 10 animals were combined. The recorded values indicated in Table I for liver and kidneys 217 days after injection of uranium accordingly are not significantly different from background.

The mean values of the percentage distribution 24 hours after injection were as follows: liver, 2.3%; spleen, 0.6%; kidneys, 26%; skeleton, 12%; urine, 46%; faeces, 1.3%.

The uranium distribution in mice is in fairly good agreement with that in piglets. Since, however, we studied only two piglets no detailed comparison is feasible. Table II shows the uranium concentration in piglets one week after injection of 180 $\mu\text{g.}$ uranium as uranyl tricarbonate into an ear vein.

TABLE II
UPTAKE IN SOME ORGANS OF PIGLETS FOLLOWING
INTRAVENOUS INJECTION EQUIVALENT TO 180 $\mu\text{g.}$
NATURAL URANIUM

Animal	Liver		Spleen		Kidneys	
	$\mu\text{g.}$	$\mu\text{g./g.}$	$\mu\text{g.}$	$\mu\text{g./g.}$	$\mu\text{g.}$	$\mu\text{g./g.}$
1	8.0	0.014	1.7	0.048	38	0.30
2	6.4	0.010	1.6	0.039	36	0.30

The fractions of the dose taken up in the various organs are consistent with those reported by Bernard and Struxness (1957) for human subjects. We have not studied in pigs the interesting question of the concentrations as a function of time after the injection.

Discussion

Our observations differ in some respects from findings previously reported in the literature (Tannenbaum *et al.*, 1951). The concentrations recorded by Tannenbaum and his colleagues are somewhat higher than ours for bone tissue, but considerably lower for the spleen. We agree about uranium uptake by the liver, kidneys, urine, and faeces. In our studies, the splenic uptake was initially much lower than the renal, but then gradually approached the mean renal values, so that after two months the spleen and kidney concentrations were approximately equal. At the end of a little more than six months the concentrations in the spleen exceeded those in the kidneys by a factor of 10.

In reported experiments on human subjects (Bernard and Struxness, 1957), the observed ratio between the kidney and spleen concentration has been approximately the same as that noted by Tannenbaum and his colleagues (1951) in mice. But tetravalent uranium (UCl_4), following intravenous injection in humans, accumulated more in the spleen than in other organs (Bernard and Struxness, 1957). Bernard and Struxness did not, however, report the amounts of uranium injected. Since UCl_4 is not very soluble in blood, a substantial proportion may be assumed to undergo agglomeration and hence to be more absorbed by reticulo-endothelial tissues. Even so, the concentration in the spleen is surprisingly high by comparison with the liver. We can offer no explanation of the discrepancies between our data and previous observations. The autoradiographic findings, however, confirm the relatively high splenic uptake.

The average uranium concentration in the kidney provides little indication of the distribution in that organ. It is evident from autoradiographs of whole-body sections that the cortex appears to accumulate far more uranium than the medulla. Indeed, the difference in this respect becomes more marked as time goes on, since the rate of disappearance after the injection is much faster for the inner parts of the kidney than for the outer cortex.

The distribution of uranium in mouse kidneys that emerges from our autoradiographic investigations closely accords with that found by Tannenbaum and his colleagues (1951). It is consistent, moreover, with the localization of renal lesions following injection of natural uranium, as reported by Barnett and Metcalf (1949). Barnett and Metcalf found that the first lesions detectable in the rat after inhalation of small amounts of uranyl hexafluoride were localized exclusively in the proximal, convoluted tubules in the arcuate and

subarcuate zones, *i.e.*, at the corticomedullary junction. These effects appeared after as short a time as three to four days. The explanation for the initially greater deposit in the inner cortex and the higher retention in the outer is not known. There are, however, certain differences in the blood supply of the peripheral and the juxtamedullary glomeruli that might have a bearing on the observed phenomena. The latter glomeruli are larger than the former, and their blood flow per unit time is greater since the efferent vessels of the juxtamedullary glomeruli are of wider calibre than their afferent vessels. Further, the efferent arterioles of these glomeruli terminate in the arterioles rectae spuriae, whereas those of the outer glomeruli empty into the capillary bed of the cortical labyrinth (Trueta, Barclay, Daniel, Franklin, and Prichard, 1947).

Uranium causes ischaemia of the renal cortex. Twenty-four hours after an intravenous injection of 200 μg . uranium the kidney is as pale as the perirenal fat; the cortex is paler than the renal pelvis and, in this respect, conspicuously differs from the kidneys of control animals. Even a uranium dose as low as 25 μg . leads, within 24 hours, to such ischaemia that the difference in colour is evident to the naked eye. Microscopic examination of sections stained with Sudan IV demonstrates that the observed paleness is not due to fatty degeneration. The presence of genuine ischaemia is quite clear from the fact that, on comparison with control kidneys, there is a manifest paucity of red cells in the capillaries and glomeruli, while intravenously injected India ink causes very little darkening of the cortex (Walinder, 1965, unpublished results). Trueta and his colleagues (1947) have found that in mice, concomitantly with the vasoconstriction attendant upon certain pathological conditions, the renal circulation is diverted, wholly or in part, from the cortical to the juxtamedullary glomeruli. Should a similar phenomenon accompany the ischaemia observed by us, it would be plausible to see therein an explanation of the faster release of uranium from the arcuate and subarcuate zones than from the outer cortex.

Casarett (1964) noted increasing ischaemia of the renal cortex following a single intravenous injection of ^{210}Po in rats. Casarett and Morrow (1964), after having injected polonium hydroxide colloid intratracheally in rabbits, found that for the kidneys the ^{210}Po concentration was greater in the proximal tubules at the corticomedullary junction than in the medulla and the outer zone of the cortex. The effects of polonium deposited in the kidney appear later than those of uranium. This seemingly delayed onset of otherwise similar effects is not surprising, in that

^{210}Po damage is due to irradiation, whereas uranium damage is chiefly attributable to toxic properties. There is, accordingly, reason to expect an earlier manifestation of uranium damage, regardless of whether the respective underlying mechanisms are identical or not.

Uranium is deposited chiefly in the distal portion of the proximal convoluted tubules. Following reabsorption of the carbonate ion the uranium is set free to affix itself to the protein of cells lining the proximal tubule. But since these combinations are reversible (Hodge, 1956) the relatively swift release of uranium from the kidneys appears likely to be a washing-out effect due, among other things, to combination of uranium with urea in a soluble complex compound. On this assumption, the effect of such washing-out would depend to a large degree on the volume of fluid passing through the nephron per unit time.

Infusion of NaHCO_3 is frequently recommended for the treatment of uranium poisoning (Dounce, 1949; Wills, 1949; Neuman, Fleming, Dounce, Carlson, O'Leary, and Mulryan, 1948; Smith, 1951). Should the above hypothesis of a washing-out mechanism, acting notably in the arcuate and sub-arcuate zones, be correct and applicable to the human organism, too, injections of HCO_3^- (possibly combined with vasodilating substances) into the renal artery via a catheter introduced percutaneously into the femoral artery would accelerate the excretion of uranium from those areas in which Barnett and Metcalf (1949) found the initial lesions in uranium poisoning. We have not studied the effect of such treatment experimentally and cannot therefore verify that NaHCO_3 does have this selective effect upon uranium absorbed in the arcuate zone.

The deposition of uranium in the proximal convoluted tubules (due to reabsorption of the carbonate ion) probably competes with the dissolving action of the urine. This is suggested by the observation of Tannenbaum *et al.* (1951) (which our results confirm) that when the amount of uranium injected is increased, the renal uptake rises disproportionately. The urine may be assumed to have a limited 'washing-out' capacity. Reabsorption of the carbonate ion and deposition of uranium take place very rapidly.

Working with rats, Jones (1965) did not find higher uranium concentrations in the inner than in the outer cortex but observed that the uranium initially deposited in the proximal convoluted tubules gradually shifted distally. This, indeed, may be expected if the uranium deposited in these tubules is subject to continuous washing-out, throughout which the competition proceeds between

soluble uranium complex compounds and deposition of insoluble uranium-protein complex compounds on the walls of the tubules. Jones studied the deposits microscopically and found that the outer cortex contained agglomerates, between which there were areas with lower concentrations of activity. (This finding is corroborated by our microautoradiographic observations in mice.)

With the microautoradiographic technique we have not been able to demonstrate conclusively any specific localization of uranium in the nephron. Twenty-four hours after the injection, uranium is present in some proximal tubules, yet many of them show no trace of activity. Minute amounts may be present in Henle's loops as well as interstitially. The glomeruli, however, apparently are not contaminated.

REFERENCES

- Barnett, T. B. and Metcalf, R. G. (1949). The pathological anatomy of uranium poisoning. Chapter 4. In *Pharmacology and Toxicology of Uranium Compounds*, Vol. I. Ed. Voegtlin, C., and Hodge, H. C., p. 207. McGraw-Hill, New York.
- Bernard, S. R., and Struxness, E. G. (1957). A Study of the distribution and excretion of uranium in man. Oak Ridge Natl. Lab. Rept. ORNL-2304.
- Casarett, G. W. (1964). *Radiat. Res.*, Suppl. 5, 246.
- Casarett, L. J., and Morrow, P. E. (1964). *Ibid.*, Suppl. 5, 175.
- Doniach, I., and Pelc, S. R. (1950). *Brit. J. Radiol.*, 23, 184.
- Dounce, A. L. (1949). The mechanism of action of uranium compounds in the animal body. Chapter 15. In *Pharmacology and Toxicology of Uranium Compounds*, Vol. II. Ed. Voegtlin, C., and Hodge, H. C., p. 951. McGraw-Hill, New York.
- Galkin, N. P., Maiorov, A. A., and Vertyatin, U. D. (1963). The Technology of the Treatment of Uranium Concentrates. *Internat. Series of Monographs on Nuclear Energy*. Div. IX. Chem. Eng. Vol. I. Pergamon Press, Oxford (Translated from Russian by R. D. M. Hegarty).
- Hodge, H. C. (1956). *Arch. industr. Hlth.*, 14, 43.
- Jones, E. S. (1965). Microscopic and autoradiographic studies of distribution of uranium in the rat kidney. Oak Ridge Natl. Lab. Rept. ORNL-3703.
- Neuman, W. F., Fleming, R. W., Dounce, A. L., Carlson, A. B., O'Leary, B., and Mulryan, B. (1948). *J. biol. Chem.*, 173, 737.
- Smith, H. W. (1951). *The Kidney*. Oxford University Press, New York.
- Tannenbaum, A., Silverstone, H., and Koziol, J. (1951). Distribution of ^{233}U in tissues of mice following injection of uranyl nitrate. Paper 7, p. 124. Tracer studies of the distribution and excretion of uranium in mice, rats, and dogs. Paper 8, p. 128. In *Toxicology of Uranium*. Ed. Tannenbaum, A. McGraw-Hill, New York.
- Trueta, J., Barclay, A. E., Daniel, P. M., Franklin, K. J., and Prichard, M. M. L. (1947). *Studies of the Renal Circulation*. Blackwell Scientific Publications, Oxford.
- Ullberg, S. (1954). *Acta Radiol. (Stockh.)* Suppl. 118.
- Wills, J. H. (1949). Characteristics of uranium poisoning. Chapter 5. In *Pharmacology and Toxicology of Uranium Compounds*, Vol. I. Ed. Voegtlin, C., and Hodge, H. C., p. 237. McGraw-Hill, New York.