polymerase-α, 100 to 500 μ*M*; and DNA polymerase-β, 125 to 500 μ*M*; and DNA polymerase-γ, 50 to 500 μ*M*). In searching for a proofreading activity in eukaryotic cells, the requirement for a high concentration of deoxynucleotide substrates may be of concern, since this may reduce the contribution of proofreading to accuracy.
5. L. A. Weymouth and L. A. Loeb, *Proc. Natl. Acad. Sci. U.S.A.* **75**, 1924 (1978).
6. M. D. Challberg and P. T. Englund, *J. Biol. Chem.* **254**, 7820 (1979); A. L. Sherman and M. L. Gefter, *J. Mol. Biol.* **103**, 61 (1976).
7. K. P. Gopinathan, L. A. Weymouth, T. A. Kunkel, L. A. Loeb, *Nature (London)* **278**, 857 (1979).
8. T. A. Kunkel and L. A. Loeb, unpublished data.
9. L. A. Loeb, T. A. Kunkel, R. M. Schaaper, in *Mechanistic Studies of DNA Replication and Genetic Recombination*, B. Alberts, Ed. (Academic Press, New York, 1980), vol. 19, p. 735.
10. U. Hibner and B. Alberts, *Nature (London)* **285**, 300 (1980); N. K. Sinha and M. D. Haimes, in *Mechanistic Studies of DNA Replication and Genetic Recombination*, B. Alberts, Ed. (Academic Press, New York, 1980), vol. 19, p. 707.
11. This study was made possible by gifts of highly purified DNA polymerases from several investigators. We thank J. W. Hockensmith and R. A. Bambara (University of Rochester, Rochester, N.Y.) for DNA polymerase-α from calf thymus, form C, purified as described by A. M. Holmes, I. P. Hesselwood, and I. R. Johnston [*Eur. J. Biochem.* **43**, 487 (1974)]; S. H. Wilson (NIH) for DNA polymerase-α from mouse myeloma [which was fraction IV purified as per Y.-C. Chen, E. W. Bohn, S. R. Planck, S. H. Wilson, *J. Biol. Chem.* **254**, 11678 (1979)]. This fraction contains both form α_1 (containing exonuclease activity) and α_2 (devoid of exonuclease activity). The relative contribution of the two forms to activity and accuracy is not known. DNA polymerase-β from mouse myeloma, also supplied by S. H. Wilson, was the homogeneous fraction V, purified as described [K. Tanabe, E. W. Bohn, S. H. Wilson, *Biochemistry* **18**, 3401 (1980)]. For both mouse myeloma DNA polymerases, a unit is described as 1 μmole of total nucleotide incorporated per hour at 37°C. The DNA polymerase-β from rat hepatoma cells (Novikoff) was a gift of D. W. Mosbaugh and R. R. Meyer (University of Cincinnati), and was the homogeneous fraction VI, purified as described [D. M. Stalker, D. W. Mosbaugh, R. R. Meyer, *Biochemistry* **15**, 3114 (1976)]. Highly purified DNA polymerase-γ from HeLa cells (DNA-cellulose fraction) was a gift from S. Spadari (Laboratorio di Genetica Biochimica ed Evoluzionistica, Pavia, Italy).

2 December 1980; revised 27 March 1981

Radioactivity Measurements of Former Military Personnel Exposed to Weapon Debris

Abstract. *Sixteen former military personnel who were present at the "Smoky" atmospheric nuclear weapon test have been investigated for internal deposits of radioactivity. Whole-body and thorax gamma-ray measurements, thorax and skeletal actinide measurements, and urinalyses for plutonium-239 and strontium-90 indicated no evidence of radioactivity in excess of that found in the general population.*

An increase in the incidence of leukemia (9 cases observed versus 3.5 expected) has been reported in a cohort of 3224 men who were present at the "Smoky" atmospheric nuclear weapon test in 1957 (*1*). Because of the relatively low mean external dose recorded for the cohort (466 mrem), it has been suggested that additional exposure from internally deposited radioactivity may have been a significant component of the total dose received (*2*). To assess the validity of this hypothesis, a small group of men who were present at the test were examined for internal deposits of long-lived radioactivity. Nineteen men were selected by the Centers for Disease Control on the basis of high film-badge readings or their opportunity for inhalation or ingestion of weapon debris, or both; 16 of the men visited Argonne National Laboratory for measurements in 1979, and three chose not to participate. The 16 ranged in age from 40 to 60 with a mean age of 46.9 ± 5.9 years; none exhibited any clinical signs of malignancy or other radiation-induced pathology. In what follows, only the outlines of our measurement techniques and the mean results are reported; detailed results are given in (*3*).

The whole-body contents of γ-ray emitters were measured with large NaI(Tl) detectors in both reclining chair and flat bed geometries (*4*). The γ-ray spectra were analyzed by a computer method of least squares. With the exception of ^{40}K, ^{137}Cs, and short-lived radon daughters, γ-ray emitters in the 16 subjects were below the limit of detection of 0.2 to 0.5 nCi (depending on energy). The mean potassium content determined from ^{40}K was 0.20 ± 0.03 percent of body weight. [One standard deviation (σ) is given for all values in this report.] For a set of 12 control men, the value was 0.19 ± 0.03 percent, whereas that for "reference man" (*5*) is 0.20 percent. The mean $^{137}Cs/K$ ratio for the 16 subjects was 8.2 ± 2.5 pCi/g, whereas that for the controls was 8.9 ± 2.4 pCi/g. Similar values have been reported for other groups drawn from the general population (*6*). The short biological half-life of ^{137}Cs (~ 110 days) (*6*) precludes any observation of even a large intake that occurred 22 years before. However, our measurements rule out the possibility that during the weapon test period these subjects inhaled and retained highly fused particles of fallout which contained ^{137}Cs (and, by inference, other fission products) in a form insoluble in body fluids.

We determined the possible actinide (^{239}Pu and ^{241}Am) contents of these subjects by two methods: (i) external counting with a large, xenon-filled proportional counter and (ii) urinalysis for ^{239}Pu. The proportional counter is sensitive to the low-energy (13 to 60 keV) photons emitted by these isotopes after α-decay. The mean counting rate observed for the subjects in the band from 16 to 26 keV with the counter viewing the lungs was 3.67 ± 0.54 count/min, whereas that from several uncontaminated controls was 3.68 ± 0.13. Similarly, with the counter viewing the skull, the mean subject counting rate was 2.07 ± 0.52 versus 2.05 ± 0.18 for controls. None of the counting rates for individual subjects differed from the mean control rate at the 90 percent (1.64 σ) level. However, external counting is a relatively insensitive means of detecting internally deposited ^{239}Pu because of the low photon abundance and severe attenuation by bone and soft tissue. An individual could contain several times the maximum permissible lung burden of ^{239}Pu (16 nCi) and still not yield a statistically significant increase in counting rate above that for the controls. These considerations do not apply to ^{241}Am, and no evidence of the 60-keV γ-ray from ^{241}Am was observed in any of the subjects.

Because of the possibility that the results of external counting for both fission products and actinides might be negative, we also collected a 24-hour urine specimen from each subject. Samples were analyzed for plutonium by isotope-dilution α-spectrometry, and the plutonium content of each sample was below the limit of detection (4.5 fCi) of our standard method (*7*). We then estimated upper limits for the body content of plutonium by applying either Langham's power function equation (*8*) or the retention function proposed by a task group of the International Commission on Radiological Protection (ICRP) (*9*) to a urinary excretion rate of 4.5 fCi/day. From Langham's equation, which relates daily urinary excretion to systemic intake, we deduce that the systemic intake was less than 1.7 nCi in August 1957 (7900 days before the urine collections). Since the use of the equation for times much longer than 5 years is known to overestimate the systemic intake (*10*), the value of 1.7 nCi must be regarded as an extreme upper limit. A limiting value for the current body content of < 200 pCi results from the use of the retention equation suggested in ICRP Publication 19 (*9*). [The urinary value was multiplied by 1.47 to determine the total excretion rate (*10*) before application of the retention equation.] These low values for plutonium content based on excretion rates

0036-8075/81/0814-0767$01.00/0 Copyright © 1981 AAAS

confirm the negative results of the external measurements of plutonium content made with the proportional counter.

The urine samples were also analyzed for ^{90}Sr by chemical separation and β-counting. The mean excretion rate of the 16 subjects was 0.63 ± 0.33 pCi/day, whereas that of seven control subjects was 0.66 ± 0.30 pCi/day. We thus infer that both groups were drawn from the same population; that is, the ^{90}Sr excreted by the test subjects arose from exposure to global fallout rather than from their presence at weapon tests.

In summary, we were unable to detect internal deposits of radioactivity in any of these 16 men in excess of normal levels found in the general population. We could only test for long-lived isotopes, but, because of their solubility in body fluids, ^{137}Cs and ^{90}Sr contribute the major portion of the dose from internally deposited fallout (*11*). Thus we have no evidence that these subjects received any significant internal dose from their participation in the "Smoky" weapon test.

R. E. TOOHEY
J. RUNDO
M. A. ESSLING
J. Y. SHA
R. D. OLDHAM
Center for Human Radiobiology, Argonne National Laboratory, Argonne, Illinois 60439
J. SEDLET
J. J. ROBINSON
Occupational Health and Safety Division, Argonne National Laboratory

References and Notes

1. G. G. Caldwell, D. B. Kelley, C. W. Heath, Jr., *J. Am. Med. Assoc.* **244**, 1575 (1980).
2. B. L. Cohen, *Health Phys.* **39**, 659 (1980).
3. R. E. Toohey, J. Rundo, M. A. Essling, J. Y. Sha, R. D. Oldham, J. Sedlet, J. J. Robinson, *Argonne Natl. Lab. Rep. ANL-80-65*, part 2, in press.
4. A. T. Keane, J. Rundo, D. R. Huff, *Argonne Natl. Lab. Rep. ANL-7960* (1972), part 2, p. 149.
5. *Reference Man* (Publication 23, International Commission on Radiological Protection, Sutton, Surrey, England, 1974), p. 312.
6. D. Newton, M. C. Eagle, J. B. Venn, *Int. J. Environ. Stud.* **11**, 83 (1977); R. G. Thomas, E. C. Anderson, C. R. Richmond, *Los Alamos Sci. Lab. Rep. LA-6898-PR* (1977), p. 5.
7. R. P. Larsen and R. D. Oldham, *Talanta* **22**, 577 (1975); I. K. Kressin, *Anal. Chem.* **49**, 842 (1977).
8. W. H. Langham, S. H. Basset, P. S. Harris, R. E. Carter, *Los Alamos Sci. Lab. Rep. LA-1151* (1950); *Health Phys.* **38**, 1031 (1980).
9. *Metabolism of Compounds of Plutonium and Other Actinides* (Publication 19, International Commission on Radiological Protection, Sutton, Surrey, England, 1972).
10. J. Rundo, P. M. Starzyk, J. Sedlet, R. P. Larsen, R. D. Oldham, J. J. Robinson, in *Diagnosis and Treatment of Incorporated Radionuclides* (International Atomic Energy Agency, Vienna, 1976), p. 15.
11. *The Effects of Nuclear Weapons* (Defense Atomic Support Agency, Washington, D.C., 1962), p. 611.
12. This work was supported by the U.S. Department of Energy under contract W-31-109-ENG-38.

23 March 1981; revised 5 May 1981

Pituitary Gastrins Occur in Corticotrophs and Melanotrophs

Abstract. *The gut hormone gastrin was identified in pituitary cells containing adrenocorticotropic hormone and α-melanocyte–stimulating hormone by region-specific immunocytochemistry and radioimmunoassays. Smaller amounts of gastrin were found in nerve fibers of the neural lobe and pituitary stalk. Since adrenocorticotropic hormone–like peptides occur in antropyloric gastrin cells, these data indicate a considerable similarity in peptide composition of pituitary and gastrointestinal endocrine cells and reinforces questions of multiple hormone production.*

Adrenocorticotropic hormone (ACTH)–related peptides were recently shown not to be confined to the pituitary but to also occur in central neurons (*1*, *2*) and in gastrointestinal gastrin-secreting cells (*2*). Immunoreactive gastrins have also been detected in pituitary extracts (*3*). By using region-specific immunocytochemistry and radioimmunoassays on microdissected pituitaries and isolated pituitary cells, we have determined that pituitary gastrins occur in cells containing ACTH and α-melanocyte–stimulating hormone (MSH) and in nerve fibers of the pituitary stalk and neural lobe.

Pituitaries from pentobarbital-anesthetized cats were dissected into anterior lobes, neurointermediate lobes, and pituitary stalks. Pig pituitaries, from a local abattoir, were microdissected into anterior, intermediate, and neural lobes as well as pituitary stalks and hypothalami. Porcine pars intermedia cells were also isolated by the method of Crine and coworkers (*4*). Specimens were frozen in liquid nitrogen and extracted by boiling for 20 minutes in redistilled water, then homogenized and centrifuged (*3*). Each pellet was reextracted in 0.5*M* acetic acid as described (*3*). Extracts were tested by radioimmunoassays specific for different sequences of gastrin-17 and of the related hormone cholecystokinin-33 (CCK-33) (*5*). Gel filtration was performed on Sephadex G-50 SF columns (10 by 1000 mm) with 0.02*M* barbital (*p*H 8.4) containing 0.1 percent bovine serum albumin being used for elution (4 ml per hour at 4°C). The fractionations were monitored by the gastrin and CCK assays (*5*). Protein was determined according to the method of Lowry *et al.* (*6*).

For immunocytochemistry, pentobarbital-anesthetized cats were perfusion-fixed with 4 percent paraformaldehyde in 0.1*M* sodium phosphate buffer, *p*H 7.4 (1.0 to 2.0 liters). Pituitaries from formaldehyde-perfused cats and from nonperfused pigs were immersion-fixed in the formaldehyde solution for 24 hours at

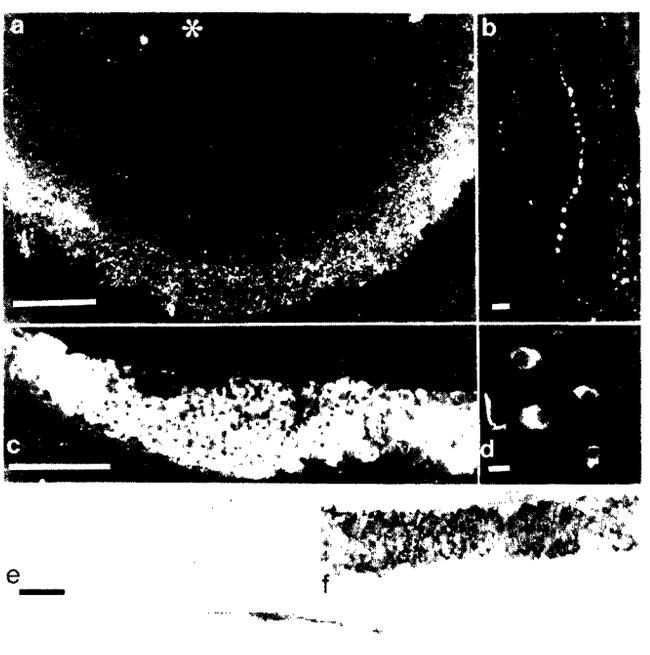

Fig. 1. Sections of cat pituitary. (a) Median eminence (scale bar, 100 μm); (b) pituitary stalk (scale bar, 10 μm); (c) intermediate lobe (scale bar, 150 μm); (d) anterior lobe (scale bar, 15 μm); and (e–g) three adjacent sections of intermediate lobe (scale bar, 100 μm). Sections (a) to (d) were stained with the COOH-terminus–specific antiserum 4562, which reacts with both gastrin-17 and CCK-33 (indirect immunofluorescence). For reasons specified in the text, the nerves seen in the median eminence (a) are chiefly CCK nerves (asterisk indicates the third ventricle), whereas the nerves detected in the pituitary stalk [note the varicose fiber in (b)] and posterior lobe and in the endocrine cells of the intermediate lobe (c) and the anterior lobe (d) store gastrin. The gastrin-storing cells and nerves also react with gastrin(6–13) antiserum 4710 but not with CCK(25–30) antiserum 4698, as illustrated for the intermediate lobe in (e) (antiserum 4698) and (f) (antiserum 4710), by means of the PAP technique; (g) is stained by gastrin-17-absorbed antiserum 4710.

0036-8075/81/0814-0768$01.00/0 Copyright © 1981 AAAS