Table 2. Mean pain relief scores for 24 patients given two 10-mg doses of morphine.

Dose	Severe pain 45 min	Severe pain 90 min	Moderate pain 45 min	Moderate pain 90 min
1	1.93	2.07	2.44	2.44
2	1.93	2.27	2.22	2.44
Difference	0.00	+0.20	−0.22	0.00

again with morphine, 10 mg, suggested that morphine following dihydrocodeine would be more effective than when given alone. Data on these studies are limited to few patients, not justifying statistical analysis, and can serve only as suggestive support.

So far as we have found, the material presented here is the first occasion where synergism in the relief of pathological pain in man has been clearly demonstrated with analgesic drugs. Attention must be called, however, to the related work of Macht (*6*). Macht worked on himself and two colleagues with experimental pain produced by the Martin method. He failed to use essential controls and arrived at the erroneous conclusion that papaverine is a powerful analgesic. He did report, among other things, that the analgesic effect of morphine is increased when it is combined with narcotine, a drug chemically related to papaverine.

In animals (*7*), evidence suggesting a synergism between morphine and drugs pharmacologically related to papaverine has been published. However, the literature contains no report on the interaction between morphine and papaverine in pathological pain, and no suggestion about the possible mode of interaction in this situation. Veldstra (*8*) has discussed synergism in general and has attempted to formulate possible explanations.

On the basis of our data, interaction among drugs in the experimental situation described does occur. No clue about the nature of this interaction is available.

In every experiment which utilizes patients who have received medication before being studied as to their response to an experimental drug, there is the possibility of drug interactions. While investigators using patients with chronic pain have certain advantages, since their experimental design is not limited by waning pain, they are nevertheless confronted by this interaction problem. Patients with chronic pain usually receive pain-relieving opiates and frequently in relatively large dosages while they are not under investigation (*10*). Thus the use of patients with chronic pain creates difficulties in evaluating the "priming" effect of a drug given for the very first time. On the other hand, when patients with postoperative pain are used, the effect of preceding anesthetics cannot be easily evaluated. The same influence can conceivably affect data on respiratory and other side effects when patients with chronic pain are used. It is not suggested that such possible drug interaction completely invalidates the results, but it is emphasized that data obtained under such conditions can be representative only of the conditions under which they were obtained. A complete assessment of the clinical characteristics of a drug therefore is possible only after the drug has been studied under various conditions with different methods (*10*).

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References and Notes

1. H. K. Beecher, *Pharmacol. Revs.* 9, 59 (1957).
2. G. H. Bishop, *J. Invest. Dermatol.* 11, 143 (1948).
3. J. S. Gravenstein and H. K. Beecher, *J. Pharmacol. Exptl. Therap.* 119, 506 (1957).
4. J. E. Denton and H. K. Beecher, *J. Am. Med. Assoc.* 141, 1146 (1949).
5. S. G. Macris and H. K. Beecher, in preparation.
6. D. Macht, N. B. Herman, C. S. Levy, *J. Pharmacol. Exptl. Therap.* 8, 1 (1916).
7. P. Angibeaud, L. Buchel, J. Levy, *Anesthésie et analgésie* 13, 848 (1956); F. Mercier and P. Marinace, *Compt. rend. soc. biol.* 145, 1340 (1951).
8. H. Veldstra, *Pharmacol. Revs.* 8, 339 (1956).
9. R. W. Houde and S. L. Wallenstein, *Drug Addiction and Narcotics Bull.* (1953), appendix F, p. 660.
10. This work was supported in part by a grant from the Medical Research and Development Board of the U.S. Army (contract No. DA-49-007-MD-76) and in part by a grant awarded by the Committee on Drug Addiction and Narcotics, National Research Council, from funds contributed by a group of interested pharmaceutical manufacturers.

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Current Strontium-90 Level in Diet in United States

Knowledge of the concentration of strontium-90 in the diet permits calculation of the equilibrium level in the human skeleton (*1*). This report (*2*) describes measurements on approximately 100 food samples. Samples of the important calcium (and therefore strontium-90), sources—that is, milk, vegetables, cereals, and tap water—are included.

Each vegetable sample (Table 1) represents 10 packages (about 3 kg) of frozen food, which in turn represent a production run at a food plant. The cereals (Table 2) were 200-g aliquots of a dozen boxes of the most common varieties. Liquid milk samples (Table 3) came mainly from cows that had grazed on unplowed land. Meat, eggs, and fish were omitted because their con-

Table 1. Strontium-90 in common vegetables from various locations, 1956–57.

Sample	Date	SU
Maine		
Peas	8/56	21.3
Western New York State		
Beans, cut green	8/56	20.2
Beans, cut green	9/56	18.4
Beans, cut green	9/56	8.6
Beans, wax	7/57	13.6
Beans, wax	8/57	11.3
Cauliflower	10/56	9.1
Corn	9/56	28.4
Spinach	6/57	1.8
Av.		13.9
Eastern Pennsylvania, New Jersey, Long Island		
Asparagus	6/56	1.2
Asparagus	5/57	1.1
Beans, cut green	12/56	4.6
Beans, cut green	9/56	8.0
Beans, lima	9/56	6.6
Cauliflower	fall/56	8.1
Peas	6/57	10.0
Potatoes, sweet	?/57	13.3
Potatoes, white	?/57	6.1
Squash	fall/56	11.5
Av.		7.3
Eastern Maryland, Delaware		
Asparagus	10/56	1.7
Beans, lima	?/56	2.9
Beans, lima	9/56	8.4
Broccoli	10/56	4.7
Broccoli	10/56	6.7
Broccoli	10/56	8.5
Corn	12/56	3.6
Peas	12/56	1.3
Av.		4.7
Tennessee		
Okra	7/57	18.0
Spinach	?	6.1
Spinach	4/57	1.2
Turnip greens	5/57	21.3
Turnip greens	2/56	7.8
Av.		10.9
Minnesota		
Corn	9/56	1.6
Peas	6/56	5.8
Av.		3.7
Washington, Idaho, Oregon		
Beans, lima	9/55	6.3
Broccoli	9/56	3.7
Corn	8/57	2.1
Peas	6/57	4.8
Peas	7/56	7.8
Peas	6/56	3.0
Potatoes	?/57	8.7
Squash	9/56	3.1
Squash	10/56	3.7
Av.		4.8
California		
Asparagus	4/57	1.8
Beans, lima	5/57	4.6
Beans, lima	9/55	10.0
Beans, lima	9/56	4.3
Broccoli	4/57	4.0
Brussels sprouts	10/56	12.0
Brussels sprouts	9/56	4.3
Brussels sprouts	12/56	2.5
Brussels sprouts	11/56	1.1
Cauliflower	10/56	28.5
Cauliflower	4/57	22.5
Spinach	3/57	13.9
Spinach	3/57	9.1
Spinach	3/57	9.5
Av.		8.5
Av. for all vegetable samples		9.4
Av. for peas, beans, corn, and potatoes		8.7

Table 2. Strontium-90 in common cereals from various locations, 1956–57.

Sample and location	Date	SU
Wheat (New York)	?/56	22.8
Wheat (Washington)	55/56	9.1
Bran (Michigan)	summer/57	8.6
Flour (Illinois)	7/56	6.7
Rice (Unknown)	?/56	4.0
Wheat (Unknown)	?/56	37.5
Oatmeal (Unknown)	?/56	5.7
Av. for all cereals		13.5

tribution to the calcium intake is trivial and because the Sr^{90}/Ca ratio is not expected to exceed that in milk by more than a factor of 2.

The chemical and radiometric procedures have been described elsewhere (*3*). The over-all yield of strontium was monitored with a Sr^{85} tracer. A representative set of six frozen vegetables was prepared according to the directions on the package, and the liquid phase was analyzed separately. No appreciable Sr^{90} is removed in the preparation of the vegetables for human consumption.

The data on U.S. milk (Table 3) include those of the Health and Safety Laboratory of the AEC New York Operations Office (*4*), extrapolated to late 1957 where necessary. The variations in Sr^{90} concentration from one farm to the next are probably related to the available calcium content of the pasture and to the average root depth of its grass. Duplicate milk samples from two nearby farms in Virginia gave 1.9 and 1.9, and 8.1 and 7.1 μμc of Sr^{90} per gram of calcium (hereafter referred to as strontium units, SU), respectively. Variations up to a factor of 2 occur from a single distribution source (Bergen County, N.J.) over a period of a month, reflecting changes in relative quantities of milk from contributing farms in successive batches. Despite these short-time variations, the average monthly value for different parts of the country is quite uniform, giving an average concentration for the country of about 6 SU. In comparison, the average level of Sr^{90} in British milk would be 7 to 8 SU in late 1957, on the basis of an extrapolation of the 1956 data (*5*).

The vegetables and cereals (Tables 1 and 2) are representative of large-acreage production. Variations from one sample to another grown in the same general area probably reflect different soil conditions. No appreciable increase in Sr^{90} from mid-1956 to early 1957 is observable from the data, as is not wholly unexpected, since an increase in Sr^{90} in the total fallout was only about 20 percent during this period.

Geographical differences in the Sr^{90} concentration appear but do not exceed two times the mean. In the diet, however, these differences are averaged out because of the nature of commercial food distribution. Some differences appear among plant types—for example, asparagus is relatively low, but among the major calcium contributors (peas, beans, and cereals), the Sr^{90} level is rather uniform.

The U.S. population obtains 85 percent of its calcium from milk, 4 percent from cereals, and 5 percent from vegetables (*6, 7*). If the average concentration of Sr^{90} in these foods in the United States in late 1957 is assumed to be 6, 15, and 10 SU, respectively, the average diet contains about 6.5 SU. In an extreme case, a vegetarian might have double this value.

Monthly integrated tap-water samples in the New York City area now carry about 0.1 μμc of Sr^{90} per liter. If an average consumption of 1 liter of water and 1 g of calcium from food each day is assumed, the contribution of Sr^{90} from drinking water appears to be negligible. If rain water were consumed, this source would still only account for about 20 percent of the daily Sr^{90} intake.

It is concluded that the Sr^{90} content in the diet of an average U.S. citizen in 1957 was about 6.5 SU, corresponding to an equilibrium base level of 1.6 SU, since the discrimination factor between diet and base appears to be about 4 (*1, 5*). If the diet concentration remains constant for a decade, the equilibrium bone level of 1.6 SU would be approached by young children. New-born children would have about half of this value on account of fetal discrimination, and adults would reach only 20 to 30 percent of the equilibrium level, because of the slow rate of exchange of the calcium in bone.

Table 3. Strontium-90 in milk from various locations, 1956–57. The numbers in parentheses in column 3 give the number of samples.

Location	Date	SU	
New Jersey (Bergen County)	9–10/57	Range	3.0–7.7
		Av.	5.5 (14)
New Jersey (other)	10/57	Av.	5.5 (4)
New York City (retail)*			5.5
New York State (Perry)*			4.5
Mohawk Valley	9–10/57	Av.	6.6 (4)
North Carolina	8/57	Av.	5.3 (4)
North Dakota (powdered)*			10.0
Mississippi (State College, powdered)*	?/56		6.5
Missouri (St. Louis, powdered)*			6.5
Oregon (Portland, powdered)*			7.0
Virginia (Rockingham County)	10/57	Av.	3.8 (4)
Wisconsin (Columbus, powdered)*			5.5
Av. for all 1957 milk			6.1

* Estimated from an analysis reported by Health and Safety Laboratory, New York Operations Office of the AEC (*4*), extrapolated to late 1957.

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References and Notes

1. W. R. Eckelmann, J. L. Kulp, A. R. Schulert, *Science* 127, 219 (1958).
2. Lamont Geological Observatory Contribution No. 302. This work was supported by the Biology and Medicine Division, U.S. Atomic Energy Commission. We acknowledge the valuable suggestions of W. R. Eckelmann, A. R. Schulert, E. Hodges, and E. Peets. R. Woehr assisted in the chemical operations.
3. H. L. Volchok *et al., Ann, N.Y. Acad. Sci.* 71, 293 (1957); H. L. Volchok and J. L. Kulp, *Nucleonics* 13, No. 8., 49 (1955).
4. M. Eisenbud, Hearings of the Joint Committee on Atomic Energy, May 27–June 3, 1957 (GPO, Washington, D.C.), pp. 554, 591.
5. R. J. Bryant, *et al.*, HP/R 2353, (Atomic Energy Research Establishment, Harwell, England, 1956).
6. United Nations Yearbook of Food and Agricultural Statistics, vol. 9, pt. 1 (1955).
7. U.S. Dept. Agr. Handbook *No. 62* (1957).

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Effect of Zinc on the Determination of Cyanide with Phenolphthalin

Determination of cyanide by the oxidation of phenolphthalin in alkaline solution to phenolphthalein in the presence of a trace of cupric salt and cyanide (*1*) is a method that has been used to determine trace amounts of cyanide in a wide variety of biological and industrial media. The determination is not specific for cyanide but is subject to interference by various oxidizing substances (*2*). Recent work on plating-room wastes in which this method was used has raised the question of the effect of zinc in such solutions. Zinc can form stable cyanide complexes which might cause negative errors.

To ascertain whether or not such errors exist (*3*), a series of known cyanide solutions was made up, and known amounts of zinc were added. This method of determining cyanide consists of adding 2 ml of the unknown to 10 ml of 0.05-percent KOH, followed by 10 ml of indicator solution. The indicator solution consists of 99.5 ml of 1-percent $CuSO_4 \cdot 5H_2O$ plus 0.5 ml of 1-percent phenolphthalin dissolved in 0.67-percent NaOH. This indicator solution is not stable and should be made up fresh every 2 hours. Absorbance is read at 553 mμ, the absorbance peak for phenolphthalein (*4*), 3 minutes after the indicator solution has been added. The calibration curve for cyanide alone is a straight line passing through zero.