CN^- or in an atmosphere of N_2 or air suggest that the formation of protein-bound MIT is not strongly dependent on the oxidative, energy-producing cycles of the cell. This is in contrast with the apparent dependence on those cycles of the formation of DIT and the concentration of iodide in the thyroid (*8*).

S. W. MAYER
F. H. KELLY
M. E. MORTON*
Radioisotope Research Unit, Veterans Administration Hospital, Long Beach, California and *School of Medicine, University of California, Los Angeles*

References and Notes

1. This work was supported in part by grant A-798 from the National Institutes of Health, U.S. Public Health Service.
2. M. E. Morton and I. L. Chaikoff, *J. Biol. Chem.* 147, 1 (1943).
3. D. M. Fawcett and S. Kirkwood, *J. Biol. Chem.* 205, 795 (1953).
4. J. B. Wyngaarden and J. B. Stanbury, *J. Biol. Chem.* 212, 151 (1955).
5. A. Taurog, G. D. Potter, I. L. Chaikoff, *J. Biol. Chem.* 213, 119 (1955).
6. K. Fink and R. M. Fink, *Science* 108, 358 (1948).
7. J. Gross and R. Pitt-Rivers, *Vitamins and Hormones*, vol. 2 (Academic Press, Inc., New York, 1953), p. 163.
8. N. Freinkel and S. H. Ingbar, *J. Clin. End. Metab.* 15, 442 (1955).

* Present address: 117 E. 8 St., Long Beach, Calif.

1 August 1955

Protection of Mouse Fetus against X-irradiation Death

The value of cysteinamine (beta-mercaptoethylamine) as a protective agent against ionizing radiations in the adult mammal was first established by Bacq (*1*) and has been confirmed by other investigators. In our laboratory, a study by Rugh and Wang (*2*) indicated that the effect of 700-r x-rays, the minimum $LD_{100/30}$ for CF_1 adult male mice, is modified by the intraperitoneal injection of 3 mg of cysteinamine 5 to 30 minutes before irradiation so that only 30-percent mortality occurs within the specified period. It was thought to be important to determine whether the protective value of this –SH compound could be transferred to the mammalian fetus that is x-irradiated *in utero* by the injection of the drug into the pregnant animal. Although the radiosensitivity of the fetus has been extensively investigated in terms of developmental abnormalities and lethality (*3*), no such protection studies on the fetus have been reported in the literature.

The animals used in this study (*4*) were CF_1 female mice that were x-irradiated on gestation days 13.5 to 19.5. Doses ranged from 300 to 1200 r, delivered at a rate of 96.5 r/min air dose as measured at the level of the gravid uterus. The x-ray facilities consisted of a Quadrocondex constant-potential therapy machine run at 210 kvp peak, 15 ma, and a distance of 50 cm from the target to the animal, with 0.28 mm Cu and 0.50 mm Al filters added. Cysteinamine was made up in physiological saline at a concentration of 3 mg/ml, 1 ml of which was administered intraperitoneally to the pregnant mouse 20 minutes before exposure to x-rays.

Each experiment consisted of three groups of mice. One control group received cysteinamine without irradiation. A second control series received x-irradiation alone; the third or experimental group of mice received both the drug and x-irradiation. After delivery of the offspring, the litters were counted daily and weighed at weekly intervals for 1 month. In cases in which the mice received a lethal dose of irradiation, litters were exchanged at birth with simultaneously dropped control litters in order that death or possible retardation of lactation in the irradiated mothers might not affect the growth and viability of the offspring. Data from cysteinamine-injected controls have in no way differed from uninjected control values.

Considering the weight at age 1 month, although the irradiated mice show an average weight difference of almost 5 g less than that of the non-irradiated controls, prior administration of the drug allows average weight very nearly equal to that of the controls (Table 1).

In Table 2 appear data from an experiment in which an exchange was made between treated litters and mothers and noninjected controls. Both irradiated groups showed a decreased birth weight below control weights with but slight difference between the two treated groups. All fetuses irradiated without cysteinamine died within the first 10 days after delivery, while those that had received prior cysteinamine injections exhibited 78.6 percent survival (protection to 1 month).

It seems reasonable to hypothesize that a reduction in litter size, particularly in the noncysteinamine-injected but irradiated groups, could be the result of their greater susceptibility to death *in utero*. In the data obtained following irradiation at 14.5 days of gestation (Table 1), the percentage values might seem to suggest a range of sensitivity favoring the cysteinamine-injected mice. However, the control and drug-injected groups are quite similar in weight, and an apparently significant weight difference exists between these two groups and those that received 300 r alone. The birth weight differences in the 700-r, 17.5-day series (Table 2) are those between the controls and both the irradiated groups. In terms of 1-month survival, however, it seems obvious that the survival of any mice in the cysteinamine-treated group provides evidence for the drug's protective effect, for none of the 66 controls survived.

As can be seen from the data on survival and weight to 1 month after delivery, cysteinamine provides some protection against x-irradiation not only for the adult mouse, but also for the fetal mouse. This protection is expressed as a weight

Table 1. Data for mice irradiated with 300-r x-rays at 14.5 days of gestation. The percentage survival to age 1 month is based on the number alive at birth.

Treatment	Av. litter	Natal mortality (%)	Av. birth wt. (g)	Survival to 1 mo (%)	Av. wt. at 1 mo (g)
Cysteinamine alone (14 litters, 136 mice)	9.7	2.2	1.70	76.0	11.74
X-rays alone (6 litters, 50 mice)	8.3	14.0	1.18	40.0	6.83
Cysteinamine and x-rays (6 litters, 55 mice)	9.1	14.5	1.37	54.5	11.44

Table 2. Data for mice irradiated with 700-r x-rays at 17. 5 days of gestation. The percentage survival to age 1 month is based on the number alive at birth.

Treatment	Av. litter	Natal mortality (%)	Av. birth wt. (g)	Survival to 1 mo (%)	Av. wt. at 1 mo (g)
Cysteinamine alone (14 litters, 136 mice)	9.7	2.2	1.70	76.0	11.47
X-rays alone (13 litters, 66 mice)	5.1	3.0	1.25	0	
Cysteinamine and x-rays (12 litters, 92 mice)	7.7	8.7	1.30	78.6*	8.60

* Data for three litters.

difference in mice that received 300 r at 14.5 days of gestation and as a reduction of the lethality following 700-r x-rays at 17.5 days' gestation. It is postulated that related –SH compounds with demonstrable protective value in adults might lead to a similar conclusion if they are applied to the fetus.

ROBERTS RUGH
HELEN CLUGSTON
Radiological Research Laboratory, Columbia University, New York

References and Notes

1. Z. M. Bacq and A. Herve, *Suisse Med.* 40, 1018 (1952).
2. R. Rugh and S. C. Wang, *Proc. Soc. Exptl. Biol. Med.* 83, 411 (1953).
3. L. B. Russell, *J. Exptl Zool.* 114, 545 (1950); S. Hicks, *Arch. Pathol.* 57, 363 (1954); J. G. Wilson, H. C. Jordan, R. L. Brent, *Am. J. Anat.* 92, 152 (1953).
4. This paper is based on work performed under contract AT-30-1-GEN-70 for the U.S. Atomic Energy Commission.
5. Cysteinamine was obtained from Harvey Blank of the E. R. Squibb Company and was known as Becaptan hydrochloride.

22 July 1955

Serum Cholesterol in Men in Basal and Nonbasal States

In comparative studies of serum cholesterol concentrations in population samples (*1*), it is difficult to assure that the conditions under which blood is drawn are exactly the same in different investigations. But what difference does it actually make if bloods are not drawn under basal, fasting conditions?

Over a period of 2 months, we drew blood on 4 to 7 mornings from each of 16 men on the staff of this laboratory (*2*). The basal fasting state was represented by several blood samples from each man; the other samples were drawn in midmorning when the men could be interrupted from their customary laboratory and desk work. The nonbasal serum in this series averaged 3.8 mg of cholesterol per 100 ml higher than the amount in the basal serum (*3*). This difference amounted to 1.9 percent of the mean basal value.

Another comparison was made with samples from male students of the University of Minnesota, 100 of whom were studied in the basal, fasting state while 300 others came in between classes several hours after a normal breakfast. On the average, the values for the nonbasal men were 3 percent higher than the values for the basal men.

Results of a more systematic study on clinically healthy men are summarized in Table 1. Cholesterol was measured in duplicate in serum from each man in the basal, fasting state and again 2 hours after a breakfast consisting of fruit, cereal with cream and sugar, two slices of toast with butter and jam, and coffee with cream and sugar. In one series of experiments (series A), 10 g of pure cholesterol were emulsified in scrambled eggs, and these "fortified" eggs were substituted for the cereal; thus the total cholesterol intake in the meal averaged 10.8 g.

In both series A and B, in which the men were relatively inactive after breakfast, the serum total cholesterol tended to rise. The mean increase at 2 hours was 2.41 percent of the basal value in series A and 1.83 percent of the basal value in series B. These changes are highly significant statistically. However, in series C, when breakfast was followed by moderately vigorous physical work (walking on the treadmill or working in the garden), the postbreakfast rise did not occur; instead, the mean value tended to fall from the basal level. The difference between the exercise and nonexercise responses is highly significant, the mean difference being 8.28 mg percent with a standard error of ± 2.25 mg percent.

To examine the effect of exercise on the response to cholesterol added to the meal, 3 experiments were performed on each of 4 healthy young men. Blood was sampled in the basal state and at 2, 3, 4 and 7 hours after breakfast in each case. In series D, the meal was the aforementioned ordinary breakfast, but in the other two sets of experiments, 10 g of cholesterol were added to scrambled eggs, which were substituted for the cereal. The subjects were sedentary in series D and E, but in series F they walked on the treadmill for 45 out of every 60 minutes. Under all conditions in the experiments of series D, E, and F, the serum cholesterol concentration tended to be higher after the meal than before; it was highest when the subjects were sedentary after they had received the 10-g cholesterol load. The data are summarized in Table 2.

The cause of the rise after breakfast when sedentary conditions were maintained cannot be ascribed to the cholesterol in the meal. In series A and D, the total increase of cholesterol in the blood was greater than the total cholesterol in the meal. The explanation for these phenomena would seem to illustrate the essential role of cholesterol in fat transport. In the sedentary state, the serum cholesterol rise must reflect a rise in lipoproteins, meeting the demand for transport of the newly absorbed fats. However, when there is physical activity during this absorption period, the enhanced rate of circulation, plus nutrient withdrawal from the blood to meet the increased metabolic needs, results in a lower serum concentration of lipoproteins and hence of cholesterol.

Table 1. Mean differences (mg/100 ml) nonbasal minus basal cholesterol values in clinically healthy men. All nonbasal bloods drawn 2 hours after breakfast. In series A and B, the subjects were sedentary between samples, but in series C they did physical work. In series B, breakfast included 10 g of added cholesterol.

Series	N	Mean (Δ)	S.D. (Δ)	S.E. (Δ)
A	51	4.92	± 11.72	± 1.66
B	73	3.95	± 11.74	± 1.37
C	15	− 3.93	± 12.95	± 3.34

Table 2. Average increases of serum total cholesterol (mg/100 ml) in 4 men after breakfast. In series D and E, the men were sedentary, while in series F they were physically active. In series E and F the breakfast contained 10 g of added cholesterol.

Time (hr)	Series D	Series E	Series F
2	4.2	9.3	7.3
3	3.2	11.5	7.8
4	3.0	13.5	4.3
7	3.7	15.0	9.3

Clearly, the difference in cholesterol concentration between basal and nonbasal blood drawn in the morning is so small that it may be negelected in most comparative studies, particularly if the nonbasal subjects are engaged in physical work. In addition to settling this point, the results cited suggest a reason for part of the difference in susceptibility to coronary heart disease that is reported in comparisons between active and inactive men (*4*).

ANGEL KEYS
JOSEPH T. ANDERSON
OLAF MICKELSEN*
Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, Minneapolis

References and Notes

1. A. Keys, *Voeding* 13, 539 (1952); A. Keys *et al.*, *Lancet* 263, 209 (1952); A. Keys, *J. Mt. Sinai Hosp. N.Y.* 20, 118 (1953); A. Keys *et al.*, *Arch. Internal Med.* 93, 328 (1954); *Metabolism* 3, 195 (1954); A. Keys and J. T. Anderson, *Natl. Acad. Sci.–Natl. Research Council Publ. No. 338* (1955), p. 181.
2. This work was aided by a research grant from the National Dairy Council, Chicago, Ill.
3. A. Keys *et al.*, *J. Clin. Invest.* 29, 347 (1950).
4. J. N. Morris *et al.*, *Lancet* 265, 1053, 1111 (1953); G. Biörck, W. Overbeck, C. Grönvall, *Cardiologia* 25, 232 (1954).
* Present address: National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md.

5 August 1955