Table 1. Appearance of agglutinating antibody in two quarters of cow No. 340 following exposure to *Salmonella pullorum* during a single nursing. Plate agglutination of milk.

Quarter	Titer	Time after exposure (hr)								
		0	2	4	6	8	24	48	72	96
Front	1/100	–	–	–	–	+	+	+	+	++
Front	1/10	–	–	+	+	++	++	++	++	++
Rear	1/100	–	–	–	–	+	+	+	+	+
Rear	1/10	–	–	–	+	++	++	++	++	++

before and after the exposures was performed by plate agglutination.

With the nine cows which were used, a total of 17 experiments were performed, nine of which showed antibody return induced by the exposure. The findings are illustrated in Table 1 which shows that the agglutination test became positive in the front experimental quarter in 4 hours, in the rear experimental quarter in 6 hours. These early antibody returns to what must have been very small injections of live bacteria appeared within reaction times which we have found characteristic of the cow's udder (*1*). The possibility exists, however, that, through some cross immunity with the species of *Salmonella* normally inhabiting the cow, an anamnestic reaction was involved. In this connection, the experiment illustrated in Table 2 is noteworthy. In this instance, the exposure to the organism by way of the calves' mouths did not induce enough antibody for a positive agglutination test until 24 hours later. Six days after the first exposure, the two experimental quarters were again negative and the experiment was repeated. This time, the reaction was more prompt, with a definite titer being recorded 7 hours after the exposure.

The mammary gland functions as an exocrine reticuloendothelial gland (*2*). This status is made more meaningful by the delineation of the process whereby the act of suckling can inject organisms into the gland and thus cause an outpouring of specific antibody in subsequent feedings. We suggest the term *diathelic* (δια, through; θηλη, teat) *immunization* for this phenomenon and the term *diathelic immunity* for the state induced.

Augmenting the well-known transmission of maternal immunity to the young via colostrum, and in some species via the placenta, this hitherto unsuspected relationship puts at the disposal of the offspring a large amount of antibody-forming tissue at the time at which its own reticuloendothelial organs are inadequate. The anamnestic response is apparently important here in that the previous exposures of the maternal tissues make augmented responses possible. It is likely that certain pathogenic species, scarcely represented in the placental or colostrum transmission because they are poor antigens, may give effective antigenic stimuli following diathelic immunization provided that there has been previous exposure earlier in the mother's life.

Contrary to many statements in the literature, effective absorption of antibody from the gastrointestinal tract does occur after the neonatal period; thus transmission of immunity with milk may be presumed to occur for the duration of nursing. There is evidence (*3*) that, in infant diarrhea at least, the absorption of unaltered protein is facilitated, an effect which would heighten the usefulness of this mechanism. The importance of natural feeding rather than artificial in the human infant must be assessed in terms of these new data as must, also, the varying weaning customs of primitive peoples. Though a definite advantage in breast feeding with regard to infection and mortality is persistently reported (*4*) in this country, it is apparent that where sanitation is conspicuously poor, the advantage is very much greater (*5*). In calves, similarly, completely artificial feeding may be used with some success only on premises where cattle have not been raised before.

Biologically considered, it is evident that through this process of diathelic immunization the mammary gland becomes a part of the bodily economy of the young. In this way, the immunity-producing tissues of the offspring are greatly augmented, and the problem of survival in the face of the ubiquity of bacterial and perhaps viral pathogens is reduced. It may even be asked whether the value of the mammary gland as means of generating protective immunity in the young may not outweigh its nutritional importance. Considering the success with which the birds, for example, have met the problem of nourishment of the young under a wide range of conditions, we feel that the origin and evolutionary survival value of the milk-producing organ of mammals may depend primarily on its protective action in disease rather than on its function in the nourishment of the young (*6*).

Table 2. Appearance of agglutinating antibody in udder of cow No. 885 at various times following two successive exposures to *Salmonella pullorum* during nursing at a 7-day interval. Plate agglutination of milk. Left quarters control, right quarters experimental.

Quarter	Titer	2 Mar. 1956 Time (hr)			8 Mar. 1956 Time (hr)			
		9	24	48	5	7	24	96
Left front	1/100	–	–	–	–	–	–	–
Left front	1/10	–	–	–	–	–	–	–
Left rear	1/100	–	–	–	–	–	–	–
Left rear	1/10	–	–	–	–	–	–	–
Right front	1/100	–	+	+	–	±	+	++
Right front	1/10	–	+	+	–	+	++	++
Right rear	1/100	–	+	+	–	±	+	++
Right rear	1/10	–	+	+	–	+	++	+++

BERRY CAMPBELL
MOHAMMAD SARWAR
WILLIAM E. PETERSEN
Departments of Anatomy and
Dairy Husbandry, University of Minnesota, Minneapolis

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6. This work was supported by a grant from the American Dairy Association.

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Strontium-90 in Man

The strontium-90 data on the retention of fission fallout in man, as reported by J. L. Kulp, W. R. Eckelmann, and A. R. Schulert [*Science* **125**, 219 (1957)], provide the first sound basis for evaluating the biological hazards from Sr^{90} on a quantitative scale. While the authors present excellent data, their conclusions are open to serious criticisms, a number of which are itemized in the following paragraphs.

1) The biological hazard of Sr^{90} is most important in human beings born since the Castle series of nuclear tests (beginning with the 1 March 1954 explosion). Thus the pertinent age group, for measurements made in 1955, is 0 to 1.5 years. It is somewhat misleading to present Sr^{90} bone retention data as an *average* value for ages 10 to 80. This is especially significant since infants show a much higher uptake of strontium than do adults.

2) Statistics on Sr^{90} retention in infants are too limited to permit careful evaluation of the biological hazard. Furthermore, it is again misleading to speak of *averages* for strontium retention in infants. Our concern should be with the fraction of infants who get, say, 10 times the average value, for we certainly do not wish to consider the radiation risk on a total basis.

3) The authors assume that their data reflect the establishment of an equilibrium condition in fallout and uptake of Sr^{90}. About a year elapsed between stratospheric injection of the fission debris and the time of bone measurement. The bomb-to-bone sequence is an intricate

one involving the possibility of hold-up in the food chains. For example, dairy cattle fed on stored herbage would contribute less Sr^{90} to dairy products than those on open range.

4) In the case of stillbirths, Sr^{90} data may be distorted by nonnutritional calcium prescribed for many pregnant women.

5) The authors continue the Atomic Energy Commission practice of reporting Sr^{90} concentrations in terms of maximum permissible concentrations (MPC) which are strictly meant to apply only to healthy, occupationally exposed adults. The MPC for children, to be consistent with the recommendations of the National Commission of Radiological Protection, ought to be 1/20 the occupational MPC.

6) Values for MPC have been revised downward steadily during the past two decades as more knowledge of the ultimate biological effect of skeletally retained radioelements has accumulated. In view of the greater radiosensitivity of infants to nuclear radiation, the global exposure involved, and the lifetime irradiation periods, it may well be that the appropriate MPC for evaluating the global Sr^{90} hazard should be 1/100 the occupational value. The MPC for Sr^{90} is based on comparison to the radium MPC, which, in turn, hinges on our experience with radium poisoning in human beings. Practically no data are available for radium retention in children and, in addition, very few radium-retention studies on human beings have been carried out over a period of 40 or 50 years.

7) In projecting their estimates of Sr^{90} retention through 1970, the authors make no allowance for additional nuclear tests. In view of the fact that the British will test weapons in the megaton range within a few months and the Soviets may overcome their continental proving ground limitation so that a Castle series of tests may be undertaken shortly, it seems naive to assume a vacuum in testing from 1956 to 1970.

In addition to these seven points, one should consider the role of concentration factors in fallout, the selectivity of global fallout, the possibility of different fallout patterns for bomb debris injected into the stratosphere at points other than the U.S. and U.S.S.R. test sites as well as the influence of different substrata on fallout phenomenology. Nor should one neglect the possibility of ecological upset owing to concentration of radioelements in nature.

Any meaningful evaluation of the Sr^{90} hazard must seek to assess the risk of excessive radiation exposure to the most radio-sensitive groups of the total population. Because of the global nature of the fallout, the problem of risk-evaluation should be undertaken on an international basis. No governmental group within the United States should undertake to assume or calculate risks for peoples of foreign lands. The United Nations has established a committee to investigate the biological effects of nuclear fallout, and it is to be hoped that technical reports will be forthcoming soon. Then attention may be focused on weighing the probable risks of future bomb tests, and it may be possible to fix a limit to the annual testing of nuclear weapons to keep stratospheric pollution within safe limits.

It is salutary that the Atomic Energy Commission has sponsored such high-quality scientific research and even more hopeful that phases of this work are emerging from the classified category. Independent analyses of the problem, such as those appearing in the *Bulletin of the Atomic Scientists,* now rest on a more solid foundation of fact than was heretofore possible.

RALPH E. LAPP
Arlington Towers, Arlington, Virginia
19 February 1957

Although we share Ralph Lapp's concern for the seriousness of the Sr^{90} problem for the world population, we wish to dissent from some of his interpretations of our data.

1) We quite agree that momentarily the biological hazard is greatest for young children. We do not see how a discussion of the average concentration of Sr^{90} in adults is *misleading* when we give all the individual data, as well as the averages of 10-year-age intervals, and definitely conclude that "children have 3 to 4 times more strontium-90 per gram of calcium . . . than adults."

2) We did not conclude that the present data permit "careful evaluation of the biological hazard" in children. In fact, we made it clear that many more data are urgently needed. The important statistical quantities, of course, are the mean and the standard deviation.

3) We clearly pointed out that the present situation does not represent equilibrium but that reasonable predictions can be made of what the equilibrium situation may be. By examining the steps in the bomb-to-bone chain, we were able to conclude that the quantity of Sr^{90} in human bone is approximately that predicted from our knowledge of the total fallout and the fractionation factors in the chain. Actually, the time scale of importance is on the order of a year, and in this period the milk appears to be fairly well equilibrated with the soil. When milk is the major source of calcium in the diet of young children, the children will likewise approach a transient equilibrium.

4) The data on stillborns did not involve the average predicted for ultimate equilibrium.

5) We most emphatically did not present our data in maximum permissible concentrations for several reasons, not the least of which is the current debate among competent medical scientists on what this value should be. We reported all our data in absolute units of micromicrocuries of Sr^{90} per gram of calcium. We discussed the data relative to the one official Sr^{90} level existing at the time we wrote the article—that is, the maximum permissible concentration for industrial workers stated in the *National Bureau of Standards Handbook* No. 52.

6) The setting of the maximum permissible concentration is not in our sphere of scientific competence. This was not one of our conclusions.

7) We could have calculated the average concentration of Sr^{90} in man in 1970 either by using the known number of atomic tests to date or by assuming some unknown arbitrary number. We chose the former and clearly stated our assumption. The point here was to show what will ultimately get into man from a known quantity of debris produced. It was not our intention to calculate how much might be present in man by 1970 assuming some grave political situation.

It is hoped that current experimental work in this laboratory and elsewhere will make it possible to provide information on some of the other problems which Lapp and others have raised. Although there will remain much area of debate, new data to be published shortly will place some further limits on the area of speculation. In reporting the laboratory data on this controversial and globally important subject, we have tried, and will continue to try, to present it as objectively as possible, so that the scientist-citizen such as Lapp may discuss the sociopolitical problem in as well informed a manner as possible.

J. L. KULP
W. R. ECKELMANN
A. R. SCHULERT
Lamont Geological Observatory, Columbia University, Palisades, New York
3 April 1957

Role of 5-Hydroxytryptamine in the Inflammatory Process

Benditt *et al.* (*1*) revealed that 5-hydroxytryptamine, as well as histamine and heparin, is present in mast cells. They also found that edema, following administration of egg white, is induced by liberation of 5-hydroxytryptamine from the mast cells and that histamine has a lesser role in the formation of