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REVIEW OF THE UNITED STATES ARMY WHOLESOMENESS OF IRRADIATED FOOD PROGRAM (1955 - 1966)

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Abstract — Résumé — Аннотация — Resumen

REVIEW OF THE UNITED STATES ARMY WHOLESOMENESS OF IRRADIATED FOOD PROGRAM (1955-1966). The United States Army has been actively engaged in a comprehensive program to study many questions, previously unanswerable, regarding the use of ionizing radiation for the preservation of food. This paper reviews data regarding the wholesomeness (toxicological, nutritional and, in part, microbiological safety) of irradiated foods.

The long-term feeding studies have been completed, and it has been demonstrated that irradiated foods are as wholesome and, in general, as acceptable as conventionally processed foods. Data were obtained through the efforts of more than 30 academic, commercial and government laboratories, and include results from the feeding of 21 irradiated foods (meat, fish, fruits and vegetables) to over 15000 mice, 5000 parent generation rats, 300 dogs and 37 monkeys.

The test foods were usually irradiated to 2.79 and 5.58 Mrads with spent fuel rods, ^{60}Co or 10-MeV electron sources, and were stored for a minimum of three months at room temperature before they were fed. Control, non-irradiated foods were stored frozen until fed. Diets containing 35% (dry weight) of the test food were fed to two different species for two years. Growth, reproduction, lactation, hematology, longevity, histopathology and carcinogenicity were studied. To study carcinogenicity more specifically, mice were fed 100% irradiated diets for two years. Other studies included induced radioactivity, nutrient stability and adequacy, tissue enzyme levels, digestibility, vitamin K nutrition and chemical changes. Human subjects were fed fifty-four different irradiated (9.3 krads-3.7 Mrads) foods in diets which contained 32-100% irradiated calories for two-week periods.

The conclusions arrived at were that: (a) Foods irradiated with gamma rays or 10-MeV electrons to 5.6 Mrads are as wholesome as non-irradiated foods; (b) In general, vitamin losses in irradiation processing are comparable to losses in thermal processing; (c) There is no detectable induced radioactivity in foods irradiated with ^{60}Co or with 10-MeV electrons; (d) Irradiated foods are, in general, as acceptable as non-irradiated foods.

In the light of these conclusions, the United States Food and Drug Administration has approved irradiation of the following foods: bacon with 4.5 Mrads – ^{60}Co or 10-MeV electrons; wheat and wheat products with 50 krads – ^{60}Co; potatoes with 10 krads – 2-MeV electrons. Other petitions are pending or are being prepared.

APERCU DU PROGRAMME D'ETUDES DE L'ARMEE DES ETATS UNIS SUR LA COMESTIBILITE DES PRODUITS ALIMENTAIRES IRRADIES (1955-1966). L'Armée des Etats-Unis s'occupe activement de l'exécution d'un programme général de recherches sur les nombreuses questions non encore résolues touchant l'utilisation des rayonnements ionisants pour la conservation des produits alimentaires. L'auteur examine dans le présent rapport les données relatives à la question de la comestibilité (sécurité toxicologique, nutritive et, en partie, microbiologique) des produits alimentaires irradiés.

Les études à long terme d'alimentation ont été faites; elles ont démontré que les produits alimentaires irradiés sont aussi comestibles, et dans l'ensemble aussi acceptables, que les produits traités selon les procédés classiques. Les données ont été obtenues grâce aux travaux de plus de 30 laboratoires universitaires, commerciaux et gouvernementaux et comprennent les résultats d'expériences sur plus de 15000 souris, 5000 rats d'une même souche, 300 chiens et 37 singes, au moyen de 21 produits alimentaires irradiés (viandes, poissons, fruits et légumes).

En général, les produits alimentaires utilisés ont été irradiés à 2,79 et 5,58 Mrad avec un barreau de combustible épuisé, des sources au ^{60}Co ou des sources d'électrons de 10 MeV, et ont été stockés pendant un minimum de trois mois à la température ambiante avant d'être donnés aux animaux. Des produits alimentaires témoins non irradiés ont été conservés par congélation jusqu'à leur utilisation. Deux espèces différentes ont été nourries pendant deux ans avec des aliments contenant 35% (en poids sec) de denrées irradiées. L'auteur a étudié la croissance, la reproduction, la lactation, l'hématologie, la longévité, l'histopathologie et la carcinogénicité. Afin d'étudier plus spécialement la carcinogénicité, il a soumis pendant deux ans des souris à un régime alimentaire constitué à 100% par des produits irradiés. D'autres études ont porté sur la radioactivité induite, la stabilité et la valeur des éléments nutritifs, la teneur en enzymes des tissus, la digestibilité, l'action de la vitamine K sur la nutrition et les modifications chimiques. On a alimenté des êtres humains pendant des périodes de deux semaines au moyen de 54 produits alimentaires irradiés différents (9,3 krad à 3,7 Mrad), la proportion de calories irradiées dans les régimes alimentaires variant de 32 à 100%.

L'auteur est arrivé aux conclusions suivantes: a) Les produits alimentaires irradiés par des rayons gamma ou des électrons de 10 MeV à 5,6 Mrad sont aussi comestibles que les produits alimentaires non irradiés; b) En général, les pertes en vitamines dues au traitement par irradiation sont comparables aux pertes résultant du traitement thermique; c) Il n'existe aucune radioactivité induite détectable dans les produits alimentaires irradiés au ^{60}Co ou avec des électrons de 10 MeV; d) Les produits alimentaires irradiés sont en général aussi acceptables que les produits non irradiés.

A la lumière de ces conclusions, le service de contrôle des produits alimentaires et pharmaceutiques des Etats-Unis a approuvé le traitement des produits alimentaires suivants: lard, 4,5 Mrad, ^{60}Co ou électrons de 10 MeV; blé et produits dérivés, 50 krad, ^{60}Co; pommes de terre, 10 krad, électrons de 2 MeV. D'autres demandes sont en cours d'examen ou de préparation.

ОБЗОР ПРОГРАММЫ АМЕРИКАНСКОЙ АРМИИ ПО ВОПРОСУ СОХРАНЕНИЯ ВКУСОВЫХ И ПИТАТЕЛЬНЫХ КАЧЕСТВ ОБЛУЧЕННЫХ ПИЩЕВЫХ ПРОДУКТОВ (1955 – 1966 г.г.). Армия США широко изучала многие вопросы, касающиеся применения ионизирующего облучения для сохранения пищевых продуктов. Рассматриваются данные, отвечающие на вопрос о сохранении вкусовых и питательных качеств (с точки зрения токсикологии, питательности и, частично, микробиологической безопасности) облученных пищевых продуктов.

Было завершено изучение результатов длительного кормления животных и показано, что облученные пищевые продукты сохраняют свои качества в той же степени, и, как правило, так же приемлемы, как и пищевые продукты, обработанные обычным способом. Данные были получены благодаря усилиям более 30 университетских, коммерческих и правительственных лабораторий и включают в себя результаты кормления облученными пищевыми продуктами (мясо, рыба, фрукты, овощи и др. – всего 21 вид) 15 000 мышей, 5 000 родительских поколений крыс, 300 собак и 37 обезьян.

Как правило, продукты были облучены дозами до 2,79 и 5,58 мегарада. Источниками облучения служили отработавшие топливные стержни, установки с кобальтом-60 или электронные источники мощностью 10 Мэв. Перед скармливанием продукты хранились при комнатной температуре не менее 3 месяцев. Контрольные, т.е. необлученные пищевые продукты хранили в замороженном виде до момента скармливания. Рацион, содержащий 35% (сухой вес) испытываемых пищевых продуктов, скармливали двум различным видам в течение двух лет. Изучались рост, размножение, лактация, гематология, продолжительность жизни, гистопатология и канцерогенния подопытных животных. С целью получения возможностей для более специального изучения канцерогенни мышам в течение двух лет скармливали рацион 100%-ного облучения. Другие исследования включали индуцированную радиоактивность, питательную стабильность и адекватность, уровни тканевого энзима, усвояемость, наличие витамина К и химические изменения. Люди, в отношении которых проводились эксперименты, в течение 2-х недель получали в пищу 54 различных вида облученных (9,3 килорад – 3,7 мегарад) пищевых продуктов, их рацион содержал 32 – 100% облученных калорий.

На основе опытов были сделаны следующие выводы:

а) пищевые продукты, облученные гамма-лучами или электронами мощностью 10 Мэв до 5,6 Мрад, сохраняют свои вкусовые и питательные качества в той же степени, что и необлученные; б) как правило, потери витаминов в процессе облучения аналогичны потерям витаминов в процессе термической обработки пищевых продуктов; в) в пищевых продуктах, облученных с помощью кобальтовой установки (кобальт-60) или электронами мощностью 10 Мэв, нет заметной индуцированной радиоактивности; г) облученные пищевые продукты, как правило, так же приемлемы, как и необлученные.

В соответствии с этими выводами американская администрация, ведающая пищевыми продуктами и лекарствами, одобрила употребление в пищу следующих продуктов: бекона, облученного дозой до 4,5 Мрад с помощью установки кобальт-60 или электронами мощностью 10 Мэв; пшеницы и продуктов из нее, облученных дозой до 50 килорад с помощью установки кобальт-60; картофеля, облученного дозой до 10 килорад электронами мощностью 2 Мэв. Другие сведения находятся в стадии подготовки.

PROGRAMA DEL EJERCITO DE LOS ESTADOS UNIDOS RELATIVO A LA COMESTIBILIDAD DE LOS ALIMENTOS IRRADIADOS. El ejército de los Estados Unidos ha emprendido la ejecución de un amplio programa encaminado a dilucidar una serie de cuestiones suscitadas por el empleo de las radiaciones ionizantes para la conservación de alimentos. En la memoria se exponen algunos datos relativos a la cuestión de la comestibilidad de los alimentos irradiados (seguridad desde el punto de vista de la toxicidad, de la nutrición y, en parte, de la microbiología).

Concluidos ya los prolongados estudios sobre el consumo de esos alimentos por animales, se ha demostrado que los alimentos irradiados son tan comestibles y, en general, tan aceptables como los tratados por procedimientos clásicos. Los datos se han obtenido gracias a la colaboración de más de 30 laboratorios de instituciones docentes, empresas comerciales y organismos oficiales, y comprenden los resultados de estudios sobre el consumo de 21 productos alimenticios irradiados (carne, prescado, frutas y verduras) por más de 15000 ratones, 5000 ratas de la misma progenie, 300 perros y 37 monos.

En general, los alimentos utilizados para esos estudios recibieron dosis de 2,79 a 5,58 Mrad obtenidas por medio de combustible agotado, cobalto-60 o fuentes de electrones de 10 MeV; antes de darlos a los animales se almacenaron durante tres meses, como mínimo, a la temperatura ambiente. Los alimentos no irradiados utilizados como testigo se mantuvieron congelados hasta el momento de su consumo. Durante dos años se administraron dietas con el 35% (en peso seco) de alimentos irradiados, a dos especies diferentes. Se estudió el crecimiento, la reproducción, la lactación, la hematología, la longevidad, la histopatología y la carcinogénesis. Para examinar más a fondo este último punto, durante dos años se administraton a ratones dietas con el 100% de alimentos irradiados. También se estudió la radiactividad inducida, la estabilidad y suficiencia de las sustancias nutritivas, la concentración de enzimas en los tejidos, la digestibilidad, la riqueza en vitamina K y las alteraciones químicas. Durante períodos de dos semanas se administraron a seres humanos 54 alimentos irradiados diferentes (9,3 krad - 3,7 Mrad) en dietas cuyos componentes portadores de calorías estaban irradiados en la proporción de 32% a 100%.

Se llegó a las siguientes conclusiones: a) los alimentos irradiados con rayos gamma o con electrons de 10 MeV, en dosis de 5,6 Mrad como máximo, son tan comestibles como los alimentos no irradiados; b) en general, las pérdidas de vitaminas por irradiación son análogas a las que produce el tratamiento térmico; c) en los alimentos irradiados con cobalto-60 o con electrones de 10 MeV no existe radiactividad inducida detectable; d) los alimentos irradiados son, en general, tan aceptables como los no irradiados.

En vista de estas conclusiones, la autoridad competente de los Estados Unidos ha aprobado la irradiación de los siguientes alimentos: tocino, dosis de 4,5 Mrad, cobalto-60 o electrones de 10 MeV; trigo y derivados, dosis de 50 krad, cobalto-60; patatas, dosis de 10 krad, electrones de 2 MeV. Se están estudiando o tramitando otras autorizaciones.

The process of pasteurizing or sterilizing foods for extended storage in essentially their fresh state by treatment with ionizing radiations has reached a stage of development, after more than ten years of intensive investigation, that is stimulating interest and creating an optimism for the future on an international level. However, the concept of radiation sterilization is not new. The lethal effects of ionizing radiations on microorganisms was reported shortly after the discovery of X-rays by Roentgen in 1895. Although a patent was obtained as early as 1930 for the preservation of food by ionizing radiations (1), it was not until the early 1940's that serious considerations were given toward investigating the feasibility of such a process. The first significant publication in this regard was reported in 1947 by Brasch and Huber (2) and was followed by an extensive series of publications by Proctor and Goldblith, Brasch and Huber and others in the United States, as well as by Hannan and Shepard and others in Great Britain. Hannan (3), in his monograph on food preservation, lists over 400 pertinent references covering the period from 1947 to 1955.

After the initial investigations had demonstrated the feasibility of preserving foods by ionizing radiations, a comprehensive program for its development was initiated by the U. S. Army in 1953. A part of this program, which was under the sponsorship of the Office of The Surgeon General, was that of determining the wholesomeness (toxicological, nutritional and, in part, microbiological safety) of irradiated foods. Prior to this time, only a meager amount of data were available for evaluating the possible toxicity of irradiated foods to mammals. Animal feeding studies by Narat (4) as well as by DaCosta and Levenson (5) had shown that growth or reproduction, respectively, was depressed in such a way as to suggest vitamin deficiencies. Poling et al. (6) reported on the results of observing over 2 600 rats representing three generations of animals which had been fed a diet containing two Mrep irradiated beef (60% of the dietary calories). The observed reduced fertility and viability in the male rats was corrected by vitamin E supplementation.

This briefly was the state of knowledge on the wholesomeness of irradiated food at the start of the U. S. Army's wholesomeness program. Because of the many excellent published reviews and symposia documenting the progress made in food irradiation processing, as well as in the wholesomeness studies, individual references will be cited only if they are specifically discussed (7 - 14).

Experimental procedures

The general procedures for the feeding of irradiated foods are shown in Table I. At least two species of animals were used for each food tested. Test foods were irradiated to 2.79 and 5.58 Mrads with spent fuel rods, cobalt-60, 1-2 or 10 MeV electrons. Nonirradiated (control) foods were stored frozen and irradiated foods were stored at room temperature for at least three months before being added as 35% dry solids to a nutritionally adequate diet. Parameters studied during the long-term feeding program were growth, food utilization, reproduction, lactation, hematology, longevity, histopathology and carcinogenicity. Reproduction was observed for four generations in rats and for as many litters as possible in dogs during the two- or three-year tests. Monkeys were not bred. In the mouse carcinogenicity studies, the animals were not bred and the parameters studied were growth, longevity and tumor incidence frequency. Histopathologic observations were conducted by the contracting institution conducting the feeding study, and duplicate sets of fixed tissues and slides were sent to the Armed Forces Institute of Pathology for review and compilation of summary statements (15 - 18).

Acute toxicity feeding studies

In order to assess the suitability of various foods for irradiation and for possible long-term feeding studies, forty-six food items were tested in weanling rats for eight weeks. During this feeding period growth, feed efficiency and any outward signs of obvious toxicity were recorded. Gross pathologic examinations were made at the termination of each study. The foods which were tested are listed in Table II.

Only three of these foods, gelatin dessert powder, vanilla dessert powder and raisins, were unsatisfactory. Irradiated gelatin dessert powder consistently reduced growth rate of rats. Subsequent evaluations had shown that irradiated sucrose was the responsible component. Irradiated gelatin dessert powder and sucrose resembled heat-carmelized sugar in odor and appearance. When heat-carmelized sucrose was

TABLE I

General Experimental Procedures
Irradiated Food Wholesomeness Studies

Test Animals:	Rats, dogs, monkeys and mice
Feeding Period:	Two years
Irradiated and Control Foods:	Fed as 35% dry solids in a nutritionally adequate diet
Storage:	Control foods - frozen Irradiated foods - room temperature for minimum of three months
Irradiation Dose:	0, 2.79 and 5.58 Mrads
Irradiation Sources:	Spent fuel rods, ^{60}Co, 2 or 10 MeV electrons
Parameters:	Growth, food utilization, reproduction, lactation, hematology, longevity, histopathology, carcinogenicity

tested, it too significantly decreased the growth rate of rats. Growth rate inhibition by irradiated vanilla dessert powder was only of borderline significance at the 5% confidence level. This product was not tested further as was the gelatin dessert powder. Repeat 12-week feeding studies with irradiated raisins did not result in significant growth rate depression; however, growth with a 35% (dry solids) raisin diet, irradiated or not, was less than that observed with other diets (19).

Apparently, irradiation can produce growth inhibitory products in foods such as gelatin powder which contain dry sucrose. The appearance and odor of these irradiated foods are not unlike that obtained with heat-carmelized sugars or heated diets which contain carbohydrates. The growth inhibitory properties of such diets are well known. Because irradiation sterilization (3 Mrads) produces the least amount of change and vitamin destruction, it is preferred to steam for the sterilization of "dry" diets containing sucrose or glucose for germfree animal studies (20).

It is suggested that dry sugar preparations may not lend themselves to irradiation sterilization at 5.58 Mrads; however, this is not irradiation specific since heat will also produce a comparably unacceptable product.

Long-term feeding studies

From the list of foods fed in the acute toxicity studies, twenty-one representative foods were selected for the long-term, multigeneration studies. These food items are listed in Table III. They include meats, fish, vegetables and fruits, as well as flour, jam and evaporated milk. All foods were irradiated to 2.79 and 5.58 Mrads, except flour which was irradiated to 37 and 74 krads, potatoes from 7 to 40 krads and oranges to 140 and 280 krads.

TABLE II

Acute Toxicity Studies
Irradiated Foods Fed to Rats for Eight Weeks
(0, 2.79 and 5.58 Mrad)

Meats	Fish	Cereals
Chicken	Haddock	Bread
Bacon	Salmon	Cereal Bar
Beef	Shrimp	Crackers
Beef, Corned	Tuna	Macaroni
Frankfurters	**Vegetables**	Rice
Ham	Asparagus	
Sausage	Beets	**Desserts and Other**
Turkey	Brussel Sprouts	Dessert Powder (Vanilla)
	Cabbage	Gelatin Dessert Powder
Fruits	Carrots	Nut Roll
Apricots, Dried	Cauliflower	Peanut Butter
Cherries, Sour	Celery	Pound Cake
Melon	Corn	Whole Dried Milk
Peaches	Cranberries	
Pears, Dried	Green Beans	
Raisins	Green Peas	
Strawberries	Lima Beans	
	Mushrooms	
	Potatoes	
	Potatoes, Sweet	
	Spinach	

In general, there were no significant differences in the parameters studied between the animals consuming irradiated or nonirradiated foods. This is not to imply that doubtful findings had not occurred. These findings will be presented and discussed in regard to their significance to the wholesomeness of irradiated foods.

In the first long-term dog feeding study with irradiated beef, it was reported that fertility was decreased (21). Calculations suggested that the vitamin E supplementation was marginal and probably the contributing cause of the reduced fertility. Two repeat studies were designed to explore this problem. These studies had three males and fifteen females per group instead of two males and two females per group as in the previous experiment. The beef was irradiated to 5.58 Mrads with 10 MeV electrons and was fed for three years. Reproductive performance in the two repeat studies was equal to that of the control animals (22, 23). The only significant finding in one of the studies was the age at first estrus (23). First estrus was shown in the irradiated beef group at 322.8 ± 46.4 days and in the control beef group at 454.8 ± 94.0 days. Since the age in days at first estrus were equal in all of the other dog studies, the significance of this single report cannot be evaluated at this time.

Thyroiditis was reported to occur more frequently in dogs fed irradiated shrimp (24) or flour (25). In subsequent summary reports from the AFIP (15, 16, 18), reviewing the incidence of thyroiditis in 258 dogs from the wholesomeness studies, it was found that 17.4% of all the dogs had some degree of thyroiditis, but that there was no statistically significant distribution between sex, diets or dietary irradiation levels. Mongrel pound dogs were found to have a 27% incidence of thyroiditis (26). It was concluded that thyroiditis commonly occurs in dogs and is not associated with irradiated foods.

Increased spleen weights were reported in dogs fed irradiated green beans and fruit compote (27). Because of the many variables that influence spleen weights, increased spleen weights cannot at this time be unequivocally related to the ingestion of irradiated foods. Histopathologic examination of the spleens did not reveal any intrinsic changes other than pulp congestion.

Growth rate was significantly reduced in the third generation rats which were fed irradiated whole oranges (28). This growth reduction was more pronounced in the 140 krad than in the 240 krad irradiated orange group. The breeding performance in all of the whole orange dietary groups was poor. It would appear that a 35% whole orange diet is not a very satisfactory diet for rats.

While the growth rate of rats which were fed irradiated carrots was reduced, the irradiated carrot groups had a higher ratio of breedings which produced litters (29). The biopotency of the carotene in irradiated carrots was also impaired to a greater extent than could be accounted for by the decrease in β-carotene content. Subsequent studies demonstrated that the biopotency of irradiated carrot carotene was not impaired if the carrots were stored frozen for 6 months; neither was growth

TABLE III

Long-Term Toxicity Studies
Irradiated Foods Fed for Two Years[a,b]

Meats	Vegetables	Other
Bacon	Carrots	Flour[e]
Beef	Cabbage	Jam
Beef Stew	Corn	Milk, Evaporated
Chicken	Green Beans	
Chicken Stew	Potatoes[d]	
Pork Loin	Potatoes, Sweet	
Fish	**Fruits**	
Cod	Compote (Dried Mixture)	
Shrimp	Peaches[c]	
Tuna	Oranges[c,f]	

a. Doses of 2.79 and 5.58 Mrad, except flour, potatoes and oranges.

b. Fed to rats and dogs, except peaches and oranges.

c. Fed to rats and monkeys.

d. Doses of 7 to 40 krads.

e. Doses of 37 and 74 krads.

f. Doses of 140 and 280 krads.

reduced when irradiated carrots were fed after being stored frozen for 12 months. Radiation per se, therefore, was not the causative agent of the growth reduction or impairment of the carotene biopotency (30). The room temperature stored carrots sometimes had an acid odor and a jelly-like residue, suggestive of bacterial contamination which could have been responsible for the observed effects on growth and carotene utilization.

In a long-term study in which a 9-component diet supplying 100% irradiated calories was fed to rats, a significant growth decrease was reported for the females of the fourth generation (31). The real significance of this is difficult to evaluate because reproduction had fallen off in all groups, irradiated and nonirradiated diets, in the third generation. Instead of the 20-25 animals per sex per group normally compared, there were only 6 animals per sex per group available in the fourth generation. The control females of the fourth generation had a much higher feed efficiency than females of previous generations, but the feed efficiency of the fourth generation, irradiated diet females was equal to that of previous generations. Because of the different variables which confused the data for the fourth generation, it is not very probable that the irradiated food was the limiting factor.

Carcinogenicity studies

The carcinogenicity studies are listed in Table IV. These studies had the primary objective of determining whether or not carcinogens were formed in foods by irradiation. Over 15 000 mice, representing nine species, were used in studies A, B and C of Table IV. In study A, mice were fed for two years diets in which 100% of the calories were irradiated. These diets were supplemented with nonirradiated vitamins and minerals.

Significant differences were not found with diet 1 of study A between the irradiated and nonirradiated diet in growth, longevity or tumor frequency.

With diet 2 of study A, significant differences were not found in growth or longevity; however, in Swiss males, there was a significantly increased incidence of malignant lymphoma in the irradiated diet group, but this lesion was also significantly more frequent in C57 black females in the control diet group (32).

With diet 3 of study A, a heart lesion described as left auricular dilatation which sometimes ruptured was reported to occur with much greater frequency in the Cb strain fed the irradiated diet than in animals fed the nonirradiated diet (33). It was later reported that this lesion could be produced as readily with nonirradiated milk diets (34). In order to confirm the original heart lesion report, the experiment was repeated in another laboratory with almost 5 000 mice of the same stock strains (35). Not one heart lesion as originally described was found in the repeat study. From 125 000 tissue and 800 000 serial heart sections which were prepared, in addition to detailed breeding, genetic and necropsy reports, it was concluded that irradiated foods were not the cause of the left auricular dilatation. Other lesions were found, but these occurred with equal frequency in all diet groups.

In study B of Table IV, the objective was to attempt confirmation of literature reports which suggested that heated or irradiated steroids can be carcinogenic. Evidence was not found to suggest that the irradiated sterols used in this extensive study were carcinogenic even when the painted irradiated sterols were challenged with croton oil (36).

Significant differences were not observed between mice fed diets containing 20% of lipid which was extracted from 5.58 Mrad irradiated or nonirradiated bacon (37).

Supplementary studies

The supplementary studies which were conducted in support of the long-term feeding trials are listed in Table V. These studies were of importance inasmuch as they supplied data which permitted a more critical evaluation of the feeding trials and irradiated foods. Because some of these topics will be considered in greater detail elsewhere during this symposium, only results of immediate interest to wholesomeness will be discussed.

TABLE IV

Carcinogenicity Studies
Irradiated Foods

A.	Composite Diets: 100% Irradiated[a], 5.58 Mrad (Mice)	
	Diet 1:	Codfish, chicken stew, beef stew, green beans, peaches, flour.
	Diet 2:	Beef, tuna, corn, sweet potatoes, fruit compote.
	Diet 3[b]:	Pork, chicken, potatoes, carrots, evaporated milk.
B.	Sterols:	Extracts were painted, injected and fed (Rats and Mice): Beef and yeast concentrates. Pork brain, egg, vegetable oils and lard. Mixture of meat, fish, cheese and milk. 0.4 to 9.3 Mrad.
C.	Bacon Lipid, 20% in diet. 5.58 Mrad (Mice)	

a. Nonirradiated vitamins added to diets.

b. Heart lesion study.

1. Induced radioactivity: It has been determined that detectable radioactivity is not induced in foods which are irradiated with ^{60}Co or 10 MeV electrons (38, 39). Depending upon individual interpretations, this statement may or may not be valid if the food is irradiated with high energy electrons and calculated, or zero time post-irradiation induced radioactivity is considered. Calculated values, although possibly high, are, nevertheless, useful for defining the magnitude of the problem. The total yearly body burden from the consumption of diets or meats irradiated to 5 Mrads with 24 MeV electrons has been calculated to be from 0.26 mrem to 11.4 mrem, respectively (40, 41). The lower figure is based on radionuclides which have a half-life longer than 10 days and is primarily due to ^{22}Na. The higher figure is based on zero time postirradiation and is primarily due to ^{126}I. Normal yearly body burden from natural background radioactivity has been estimated to be about 150 mrems. From this type of data, it is logical to conclude that foods irradiated to 5 Mrads with 10 MeV electrons should not be a biological hazard from induced radionuclides that cannot be detected.

2. Nutrient stability: In general, it has been determined that vitamin destruction in foods by irradiation sterilization is comparable to destruction by heat processing (11). However, if one compares heat sterilization to irradiation sterilization, particularly if the diets contain sugars, then irradiation sterilization produces a much superior product (20). This is an important point to consider because it is very misleading to attempt direct comparisons between a cooked product and a sterilized product. In any event, the seriousness of the vitamin losses must be evaluated in terms of the feeding situation at hand. Vitamins could be resupplemented as required much in the same way that the milling industry is fortifying refined flour with B vitamins.

TABLE V

Supplementary Studies
Irradiated Foods

1. Induced Radioactivity
2. Nutrient Stability
3. Tissue Enzyme Activities
4. Digestibility
5. Chemical Changes
6. Vitamin K Nutrition

In this regard, losses of vitamins which are added to sterilized foods post-irradiation have not been adequately evaluated. There is some indication that fat-soluble vitamins may undergo some loss in biopotency when added directly to irradiated meat diets and to irradiated or nonirradiated animal fats (31, 42).

3. Tissue enzyme activity: Tissue enzyme activities were determined in duodenum, intestinal mucosa, organs and blood of rats after various feeding periods with radiation sterilized foods in several of the long-term studies. The only consistent observation was made in rats which were fed pork (30, 31). Liver cytochrome oxidase activity was higher in the animals which were fed irradiated pork than in those fed nonirradiated pork. The reason for this difference was not clear. Some of the data suggested that it may have been due to alteration in the oleic-linoleic acid ratio between the irradiated and nonirradiated pork (30). While the irradiated pork-fed animals had a consistently greater cytochrome oxidase activity than the nonirradiated pork-fed animals, some of the data showed that the cytochrome oxidase activity of laboratory pellet-fed male rats may be higher than that of pork-fed rats. The females fed a pellet diet had a lower cytochrome oxidase activity than those on a pork diet.

It is, therefore, a very difficult task to interpret changes in tissue enzyme activities because changes in diet or dietary components are known to influence significantly enzyme activities. Whether these changes are beneficial or detrimental can at this time only be evaluated by observing the performance of the animal over its normal life span, as was done in the long-term studies being reported.

4. Digestibility: Biologically significant changes in the digestibility of irradiated proteins, fats and carbohydrates were not found. In general, with the exception of fibrous tissues, digestibility may be reduced by irradiation but the magnitude of the reduction cannot be measured biologically.

Of interest for further study are irradiated fats. In an experiment with jejunal fistulated dogs, irradiated lard was fed by intubation (43). It was determined that the irradiated lard was absorbed to a lesser extent and remained a longer time in the stomach than nonirradiated lard. This irradiated lard had an abnormally high peroxide number (176 - 350) which may have influenced the results. From the long-term feeding studies with bacon, pork and bacon lipids, any reduction in available calories was not detectable; therefore, in spite of the conclusion that the rate of utilization of irradiated fats may be decreased, net utilization is not decreased.

5. Chemical changes: Chemical changes that take place in foods with irradiation will not be discussed at this time because they will be considered in more detail elsewhere during this symposium. The only comment of pertinence to wholesomeness which should be made is that while very extensive qualitative chemical changes are known to occur in foods when they are irradiated, the products formed have not been shown to be detrimental with foods which were tested under this program.

6. Vitamin K nutrition: The irradiated food program has made significant contributions to our knowledge of vitamin K nutrition; however, the possibility of inducing vitamin K deficiencies from the ingestion of irradiated foods is very improbable. Hemorrhagic diathesis was induced in rats with irradiated or non-irradiated meats in a laboratory-type diet which was not supplemented with vitamin K. Meats are a very poor source of vitamin K. Foods such as vegetables, which are very rich sources, can be irradiated to 5.58 Mrads without measurable loss of vitamin K (44).

Human feeding studies

Human feeding studies have been limited to short-term experiments of 15 days' duration. In the seven studies, each with 9 to 10 human volunteers, diets supplying 35 to 100% irradiated calories were acceptable and as digestible as the nonirradiated diets. Extensive clinical tests did not reveal any untoward effects (45).

Discussion and conclusions

The magnitude of the wholesomeness studies can be estimated from the total numbers of animals utilized and the number of different contracting laboratories which participated in the program. Over 15 000 mice, 300 dogs and 37 monkeys were fed the various irradiated diets for at least two years. The number of rats is more difficult to evaluate because of the many different types of studies and multi-generation programs; however, a reasonable figure would be in excess of 10 000 rats. Over 30 academic, commercial and governmental laboratories participated in this program.

Irradiation certainly did not produce any obviously toxic or carcinogenic substances in the foods which were tested. A few spectacular findings, such as the heart lesion, congenital blindness (46) and hemorrhagic diathesis were reported during the course of these studies. These findings, however, have been shown not to be related to the irradiated foods. The heart lesion was produced with a non-irradiated diet in one laboratory and not at all in another laboratory, regardless of diet. The congenital blindness was due to a genetic defect in the Texas A & M rat strain, and the hemorrhagic diathesis was due to vitamin K deficiency. In diets which were not supplemented with vitamin K, nonirradiated pork was more hemorrhagic than irradiated beef.

Nutrient destruction is known to occur, but the magnitude is comparable to that occurring by heat processing and should not present any unusual problems. Small but sometimes measurable decreases in digestion rates were not biologically significant. The decreased growth rate and carotene utilization obtained with irradiated carrots were due more to room temperature storage than to irradiation. The poor condition of the irradiated carrots may have been due to bacterial contamination.

It seems apparent that if irradiated foods must be harmful, then this toxicity in the mammal must be extremely subtle or of such low frequency rate that it would be very difficult to demonstrate experimentally. While the possibility of subtle toxicity and mutagenicity of irradiated foods should not be dismissed entirely, these possibilities should also be considered for our heat processed foods because some of the changes in irradiated foods are similar to those caused by heat.

If it can be assumed that the rat, like the mouse, is fifteen times more susceptible to the genetic effects of radiation than Drosophila (47), then would it not be reasonable to assume that somewhere during the many reproduction and feeding studies some hint of genetic or other cellular changes should have been evident? The jam and peach diets, because of their very high sugar content, should have resulted in gross adverse effects if the recent conclusions of Berry et al. (48) and Holsten et al. (49), regarding irradiated sugars, have any validity to the feeding studies being reported at this time (50,51).

In considering the wholesomeness data, it should be remembered that the irradiated foods were compared to the nonirradiated foods in such a way as to give the nonirradiated foods an overwhelming advantage. Consider the possible results if radiation sterilized foods were compared to heat sterilized foods. Consider also the possible restrictions in our diets if all nutrients, foods or other substances which are mutagenic or growth inhibiting to microorganisms, tissue cultures or Drosophila were legislated off the market-place. This is not a plea in defense of potentially detrimental foods or processes, but until data in the mammal can be presented to establish toxicity, then one should accept the voluminous negative data established with mammals, rather than data based solely on microculture techniques. Nevertheless, it should be emphasized that vigilance should be continuously maintained and experimental procedures kept abreast of our ever progressing technologies for the detection and evaluation of biological signposts which may have escaped our scrutiny.

After careful review of the extensive data amassed in the wholesomeness of irradiated food program, it can be concluded that the foods which were irradiated to doses of 5.58 Mrad with spent fuel rods, cobalt-60, or 10 MeV electrons are as wholesome as nonirradiated foods.

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DISCUSSION

B. RAJEWSKY: Have you considered the possible effects of doses as high as 100 Mrad?

N. RAICA: Doses as high as this will never be used for preserving food. Experiments have been carried out in which 45-Mrad beef was fed to rats; however, the product was so obnoxious that the animals had to be force-fed. The tests were run for about three weeks and the animals showed no toxic effects.

B. RAJEWSKY: What about long-term effects?

N. RAICA: I think the animal studies already carried out show that there is no need for great concern about the long-term effects. In my opinion there is too much concern about the micorculture effects of irradiation, whereas nothing is said about the same effects when they occur in non-irradiated food; for example, the same effects have been shown to be produced in non-irradiated wheat by normal cooking oil.

B. RAJEWSKY: Do you think that the immunological factors can be excluded?

N. RAICA: Present evidence would suggest that they can be excluded. Moreover, studies carried out with milk have shown that the allergenicity of milk proteins decreases upon irradiation.

O. KLAMERTH: Have you carried out any experiments in which animals were fed with sugar solutions or sugar-containing solutions irradiated before application?

N. RAICA: No, we have not fed animals with irradiated sugar solutions or solutions made with irradiated sugar. In one short-term feeding study, Reference [19] of the paper, both irradiation-carmelized and heat-carmelized sucrose inhibited the growth of rats.

O. KLAMERTH: Although tissue culture experiments are not conclusive for the whole animal, I would like to mention the results of experiments performed in our laboratory with human fibroblasts fed with irradiated glucose solutions or with glyoxal (50 μg/ml of medium). The result was a very marked reduction in protein and DNA synthesis. However, the cell possesses a recovery system, probably xanthine oxydase, which reduces the toxic effect of glyoxal 6 - 8 hours after application.

N. RAICA: Thank you for your interesting data regarding human fibroblasts. The HeLa cells and Strain L human fibroblasts used by Berry and co-workers, Reference [48] of the paper, were not described as possessing a system for recovery from the effects of irradiated sugar solutions in which glyoxal was reported as being the active component.

F.J. LEY: The animal feeding data which you have described were obtained with individual foods irradiated under a certain set of conditions. Do you think it is reasonable to extrapolate the data obtained to cover the same foods irradiated under different conditions; for example, at different doses, at room temperature as opposed to freezing, or with gamma rays as opposed to electrons from electrical machines?

N. RAICA: The data reported could, in general, be extrapolated to lower doses than were used in this study and to include foods irradiated at below freezing temperatures, as well as to irradiation with electrons of energies about 10 MeV. This is not to say that toxicity would necessarily develop in foods irradiated to higher doses with higher energies.

B. RAJEWSKY: I would like to say that, in irradiating different kinds of food, the irradiation energy should be adapted to the thickness and density of the food being irradiated.

G. MOCQUOT: Would you say that, with the information we now possess on the non-toxicity of irradiated foodstuffs, it is unnecessary to repeat non-toxicity experiments for each new food preparation capable of being preserved by means of irradiation?

N. RAICA: Although a wide variety of foods were tested with favourable results, our present state of knowledge does not permit us to make the general statement that all irradiated foods will be wholesome. For new foods similar to those already investigated, twelve-week feeding tests may be adequate; for others, long-term studies may be advisable.

J. MORRE: I think I can offer an explanation for the difference, referred to in your presentation, between a pure sugar, such as glucose, and one present in jam. Pure sugar has a low buffer action and a pH that varies greatly during irradiation. Sugar present in jam has a high buffer action and yields completely different degradation products.

N. RAICA: This is not necessarily the explanation in this case, because in one of the studies, Reference [49] of the paper, irradiated coconut milk supplement, or irradiated basal media, also suppressed the growth and proliferation of plant cell cultures.

P. PELEGRIN: Do you think that the application to cereals (wheat or maize) of a gamma dose of 100 - 300 krad may give rise to compounds (harmful or otherwise) such that the United States authorities would require either long- or short-term survival tests on mammals, or other kinds of tests?

N. RAICA: From the large variety of foods which were studied under widely different conditions there is no reason to assume that toxic compounds should arise in wheat or maize irradiated to 100 - 300 krad. However, this does not mean that organoleptic changes would not occur. It is quite probable that the Food and Drug Administration would require feeding studies of some sort to support petitions requesting clearance for higher doses but not necessarily for petitions concerning lower doses than those tested. I should stress that this is my personal opinion, and naturally not intended as a statement on behalf of the Food and Drug Administration.