Potential Concerns Associated with Irradiated Foods (contd)

1. Induced radioactivity
2. Microbiological safety
3. Nutritional loss
4. Toxicological safety
5. Miscellaneous

4. Toxicological Safety Concerns

Possibilities which have been suggested include

- Formation of radiation-induced toxic substances
  - Radiolytic products (RPs)
  - Unique radiolytic products (URPs)
  - Long-lived free radicals

- Which is turn could lead to adverse health effects
  - Short term e.g. illness
  - Long term e.g. mutagenicity
carcinogenicity

Evaluation of Toxicological Safety Concerns

(i) Chemical approach

- Chemical identification and toxicological characterization of radiolytic products

(ii) Functional approach

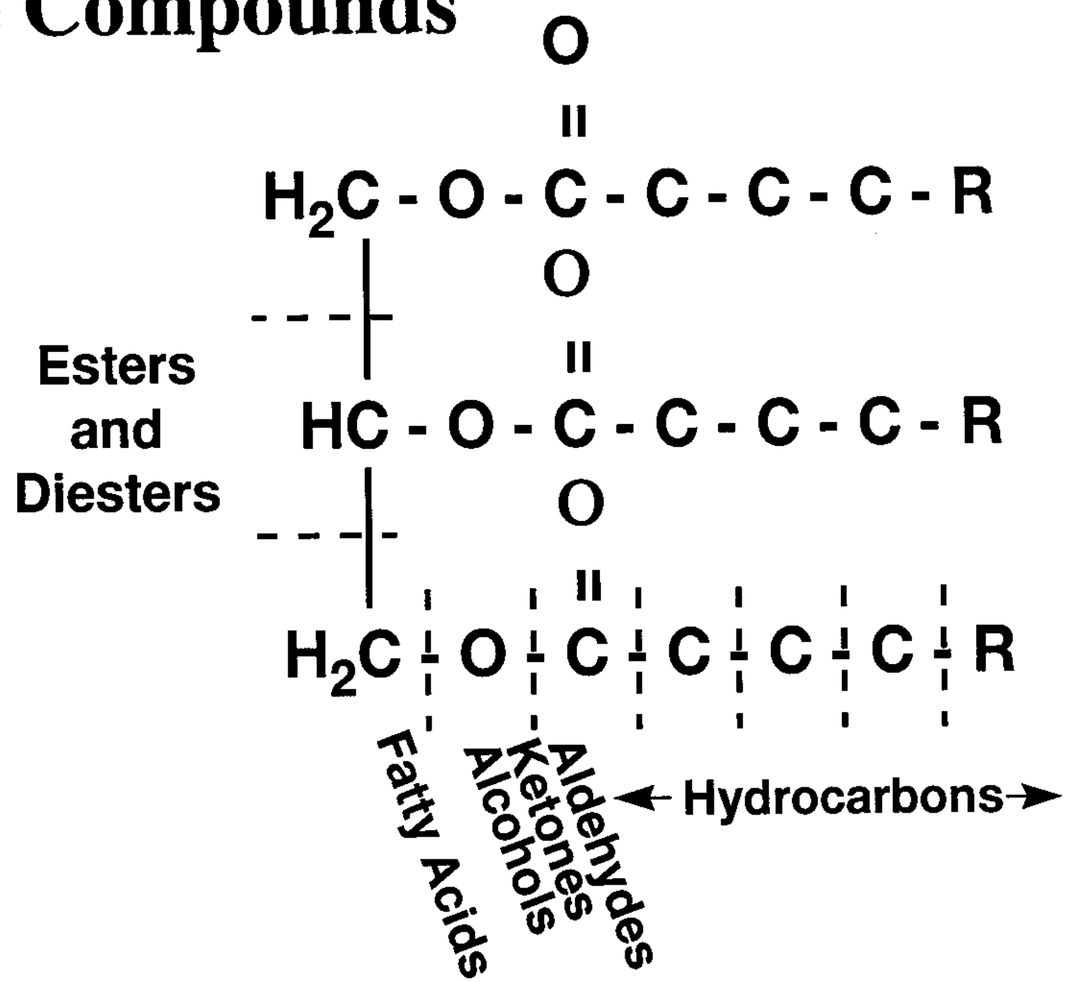
- Animal feeding tests, e.g.
  - Use of various animal species
  - Short term, long term and multigeneration effects
- *In-vitro* test systems, e.g.
  - Ames
  - SOS
- Epidemiological studies
  Correlate illness with consumption of irradiated or non-irradiated food within populations of interest
  - human (data sparse at this time)
  - animals (especially animals reared for laboratory purposes; plenty of data over last two decades)

Evaluation of Toxicological Safety Concerns
(contd)

(i) Chemical Approach

- There is enormous literature on chemical identification of radiolytic products obtained on model systems of varying complexity and on different foods
- This information was originally obtained for investigations on problems such as the "irradiation flavour" that initially develops in some meats on high dose irradiation
- These studies provide an understanding of the chemical changes in foods produced by irradiation

Volatile Compounds



FASEB EVALUATION OF IDENTIFIED COMPOUNDS IN IRRADIATED BEEF (cont'd.)

Compounds	Concentration, µg/kg (ppb)		
	Irradiated Beef	Thermally Sterilized Beef	Other Common Foods
Alkenes	0-600	0-33	Eggs, 0-3900; also found in coffee, apples, grapes, mushrooms, cheese, milk, onions, hops, tomatoes
Alkynes	4-24		Found in apples, potato chips
Dienes	15-700		Eggs, 2000
Aromatic Compounds			
Benzene	15-19	2	Eggs, 2100; Jamaican rum, 120; Haddock, 200
Toluene	50-65	48-73	Eggs, 39000; Haddock, 500; approx 30 other
Xylene	1-4	7	Found in approx 20 other foods
Alcohols			
Methanol	16-20	23-40	Passion fruit juice, 4000; Jamaican rum, 80
Ethanol	75-123	9-15	Banana, 5000; cheddar cheese, 620,000 cucumber, 200-2000; grapefruit juice, 400,000
Ketones			
Acetone	107-139	65-120	Beer, 1400; carrot, 200; cherry essence, 16,000; whole milk, 3000; whiskey, 200
2-Butanone	72-89	5-10	Butter, 160; eggs, 9600; pear, 1000; present in almost 60 other foods

FASEB EVALUATION OF IDENTIFIED COMPOUNDS IN IRRADIATED BEEF (cont'd.)

Compounds	Concentration, µg/kg (ppb)		
	Irradiated Beef	Thermally Sterilized Beef	Other Common Foods
Aldehydes			
2-Methyl pentanal	11		Found in chicken, coffee, garlic, onion, peanut, tomato
Undecanal	76		Orange, 140,000; roasted peanut, 150
Dodecanal	63		Egg, 7400; tomato, 7710; citrus oils, 760,000+
Tetradecanal	54		Roasted peanut, 230; citrus oil, 130,000+
Hexadecanal	127		Found in beef, bilberry, chicken, citrus fruits, cranberry, pork
Hexadecenal	33		Roasted peanut, 63
Sulfur Compounds			
Carbonyl sulfide	2	22-75	Horseradish, 12,000; also in chicken, parsley, cabbage
Dimethyl disulfide	3-4	7-13	Cheddar cheese, 70,000; eggs, 7400
Dimethyl sulfide	4-6		Haddock, 200,000; cheddar cheese, 1000
Ethane thiol	7-10		Boiled potato, 100-200; canned beef, 170-200
Hydrogen sulfide	2		Beef broth, 6000-8000; beer, 110; orange juice, 1600

What is the toxicological significance of these compounds present in irradiated foods?

- No radiolytic product so far identified in irradiated beef (or other meats/foods) has significant toxic characteristics as evaluated by comparison with thermally processed foods and with concentrations found naturally in a variety of other foods
- Most radiolytic products identified so far can be found in the same or similar unirradiated foods and are not unique to irradiated foods

"On the basis of the available data , the FASEB Committee (1977, 1979) concluded that there were no grounds to suspect that the radiolytic compounds evaluated in this report would constitute any hazard to health of persons consuming reasonable quantities of beef irradiated in the described manner."

(FASEB: Federation of Amercian Societies for Experimental Biology)

Occurrence of Aromatic Compounds in various Media

	µg/kg Beef				
Compound	Cooked	uncooked	Atmosphere µg/m^3	Water µg/L	Food µg/kg
Benzene			Los Angeles-(ave) 48 (max) 182; Toronto - (ave) 42 (max) 314; Zurich - 173 Gas stations (ave) 1000 (max) 11,000; Near reclamation plant - 7360; Bulk loading facilities -320-68,000; Stimulated spacecraft - 61	Highest reported in U.S. - 10.0 Canadian lake - 320 Miami - 0.1 Ottumwa - 0.1 Philadelphia - 0.2 Cincinnati - 0.3 Florida fire station - 300	Beef, canned (head-space) - 2.0 ppb; Rum-Jamaican - 120; Eggs - 2100; Haddock (stored 14 days) - 200; also detected in approximately 20 othe foods - no quantitative data available
Irrad.	15	19			
TP	2	0			
FC	3	0			
Toluene			Delft - (ave) 11 (max) 76; Los Angeles - (ave) 120 (max) 720; Netherlands-tunnel (ave) 150 (max) 240; Toronto- (ave) 140 (max) 460; Nuclear submarine 738	Highest reported in U.S. -11.0 Canadian Water - shed 375.0 Philadelphia - 0.7 Cincinnati - 0.1 Connecticut - 81-140 Effluents from textile mills	Beef, canned - 5.9; eggs 39,300; Haddock (stored 14 days) - 500; also detected but no analyzed in approximately 30 foods
Irrad.	50	65			
TP	48	73			
FC	3	6			
Xylene			Zurich - (ave) 31 (max) 91; Los Angeles (ave) 66 (max) 265; Stimu-lated spacecraft - 122	Highest reported in U.S. - 5.0 Effluents from oil refineries	No quantitative values detected in approximately 20 foods
Irrad.	4	1			
TP	7	7			
FC	1	1			

FASEB Evaluation of Identified Compounds in Irradiated Beef

Comparison of Acceptable Daily Intake (ADI) and the Quantities Obtained Via the Daily Beef Intake (DBI)

Compound	ADI		Conc. in Irrad Beef (ppb)	Daily Beef Intake (DBI)	ADI/DBI (ratio)
	Concentration	mg		µg	
Dimethyl sulfide	1.5 ppm	2.25	5	0.6	3750
Dodecanal		70	63	7.6	9210
Ethyl mercaptan	1 ppm	1.5	9	1.1	1364
Tetradecanal	3 ppm	4.5	54	6.5	692
Undecanal	5 ppm	7.5	76	9.1	824

Conclusion

- No products have been seen in amounts that would confer toxicity to irradiated foods, at doses considered appropriate for food irradiation
- For detailed data, see the original papers. The FASEB Review, 1977, 1979; the three volumes of CRC books on Food Irradiation; Recent Advances in Food Irradiation (1983, Elsevier); Food Irradiation (1986, Urbain); and Safety of Irradiated Foods (1990, Diehl) are good sources of relevant references

Evaluation of Toxicological Safety Concerns
(contd)

(ii) Functional Approach

- Animal feeding studies

  - Enormous Literature, dating back to the 1920s

  - Resulted in a number of individual and committee reviews (e.g. Barna, 1979; JECFI Report, 1981; USFDA Final Rule, 1986; ACINF Report; CAST Report, 1986; U.S. RALTECH Study, 1976)

- Comparison of thermally processed, frozen, gamma sterilized and electron sterilized chicken using male and female Sprague-Dawley rats as the test animal, in the RALTECH Study was reviewed by Thayer et al. (1984). This led to a unanimous conclusion that irradiation-sterilized chicken was wholesome and safe

Details of the RALTECH Study

- Started in 1976 and lasted 7 years (under US ARMY Medical Department)
- Cost 8 million dollars
- Consisted of 20 separate research projects, examining effect of consuming radiation sterilized chicken meat, with respect to
  - nutritional quality
  - teratogenicity
  - toxicity
  - carcinogenicity
  - reproductive performance
  - genetic toxicity
- Test species
  - dogs, rats, mice, hamsters, rabbits, fruit flies *(Drosophila melanogaster)*
- Magnitude of effort
  - 230,000 chilled eviscerated broilers used (300,000 kg of chicken meat)

Some Examples of the Results
from
RALTECH Study

Nutritional Evaluation
Growth and Protein Efficiency Ratio (PER) for Rats Fed the Test Diet

Diet	Total wt gained (g)	Total Feed consumed (g)	Total Protein consumed (g)	Calculated 28-day PER
Males				
Casein	100	294	37.2	2.69
FC	123	324	37.5	3.28
TP	115	326	40.1	2.87
γ	116	313	36.1	3.21
e^-	119	318	36.9	3.22
CLD[a]	97	307	38.0	2.55
Females				
Casein	90	288	36.3	2.48
FC	95	302	35.2	2.70
TP	104	319	38.8	2.68
γ	97	303	35.0	2.77
e^-	97	296	33.9	2.86
CLD[a]	93	324	40.1	2.32

[a] Commerical laboratory diet

- Overall result: no detrimental effect on PER of feeding irradiated chicken to rats

Ames Mutagenicity Test

- Uses *Salmonella*/mammalian microsome *in-vitro* assay to detect carcinogenic chemicals as mutagens with 90% accuracy
- 5 Mutant strains of *Salmonella typhimurium* designated TA98, TA100, TA1535,TA1537 and TA1538; which have mutation in the histidine operon making these strains unable to grow in the absence of histidine in the growth media, unless they undergo spontaneous reversion
- Each of these mutants has a fairly constant rate of spontaneous reversion; however, the mutation frequency is significantly increased when a chemical mutagen is added to the system
- Since some chemical mutagens are inactive unless they are metabolized to active form, the mammalian microsomal activation system is included in the assay

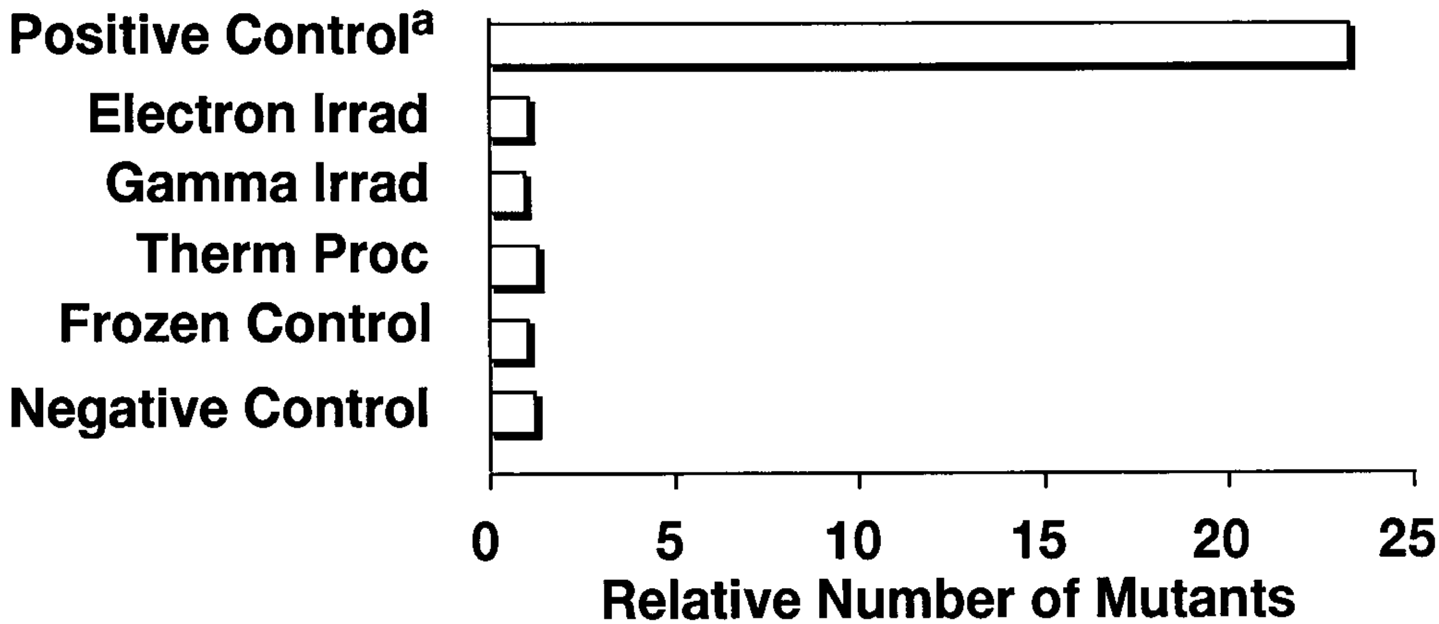
- *In-vitro* Mutagenicity test (RALTECH Study)

AMES Mutagenicity Preincubation Test Results With Frozen, Thermally Processed, and Gamma or Electron-Irradiated Chicken

Test material / mutagen / test strain	MNNG TA 1535	NQNO TA 98	BP TA 100	9-AC TA 1537	9-AF TA 1538
	Average revertant counts per plate n=6, standard deviation in parentiesis				
Mutagen control	1631 (36)	415 (44)	[illegible]	45 (5)	1205 (25)
1/3 DMSO, 2/3 H_2O	17 (20)	NA	101 (6)	5 (2)	10 (1)
Saline Solution Control	16 (1)	20 (4)	100 (7)	7 (2)	13 (2)
Chicken without mutagen					
FC	17 (4)	20 (3)	98 (13)	6 (4)	13 (2)
TP	17 (3)	20 (3)	104 (7)	6 (2)	9 (2)
γ	17 (1)	23 (2)	107 (12)	6 (3)	11 (3)
e^-	18 (3)	22 (4)	100 (11)	6 (3)	12 (4)
Chicken with mutagen					
FC	291 (181)	472 (56)	134 (11)	472 (182)	128 (14)
TP	251 (39)	469 (52)	140 (13)	475 (190)	144 (4)
γ	192 (19)	466 (61)	138 (7)	422 (145)	113 (11)
e^-	434 (269)	471 (54)	141 (15)	452 (182)	133 (15)

[a] MNNG = N-methyl-N'-nitrosoguanidine, NQNO = 4-nitroquinoline-N-oxide,
BP = benzo(a)pyrene (with S-9 mix added), 9-AC = 9-aminoacridine, 9-AF = 9-amino-fluorene (with S-9 mix added), NR
Not Run

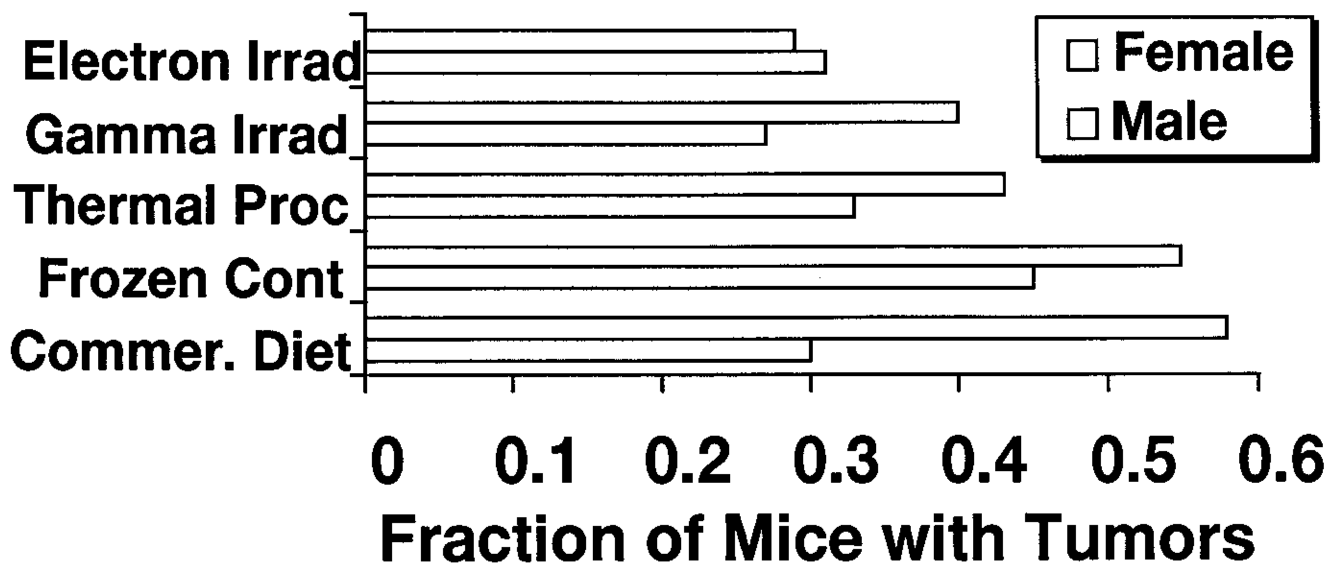
RALTECH STUDY (Genotoxicity)



a. 100 ppm tris (2,3-dibromopropyl phosphate)

- Sex-linked recessive mutations (~9000 test matings of *D. melanogaster*/diet)

RALTECH STUDY (Carcinogenicity)



- The overall tumor incidence was lowest in the groups consuming the irradiated diets

RALTECH STUDY

- Most Frequently Observed Neoplasms (Tumor Type) in Fo Mice
  - Alveologenic tumor
  - Hepatocellular carcinoma
  - Hepatocellular adenoma
  - Lymphsarcoma
  - Hemangiosarcoma
  - Mammary adenocarcinoma
  - Leiomyosarcoma
  - Pituitary adenoma
  - Reticulum cell sarcoma
  - Kidney adenoma

Feeding Studies with Radurized Chicken

- The results of three feeding studies conducted on chicken irradiated in air, at doses of 3, 6 and 7 kGy at ambient temperatures (~25°C), show that there was no toxicity associated with the feeding of the irradiated chicken

- These feeding studies are
  (i) Til, et al., 1971, feeding of irradiated chicken to beagle dogs
  (ii) de Knecht-van Eekelen et al., 1971, feeding of several generations of rats with irradiated chicken
  (iii) Proctor et al., 1971 study of carcinogenicity in mice due to feeding of irradiated chicken

Feeding Studies with Irradiated Mangoes

Horton (1976): Multigeneration study on feeding irradiated (0.75 kGy) and unirradiated Kent mango pulp to rats

- Voluntary food consumption and digestibility, normal
- Growth rate of weanling male rats, normal
- Mean daily body-weight gain, normal
- Body weight changes of "3rd-litter" females during 21-day nursing period, normal
- No adverse effect of maintaining virgin female rats on this diet for 40 days
- Hematology or blood chemistry values (hemoglobin concentration, erythrocyte count), normal
- Levels of the serum enzyme, aspartate amino-transferase, normal

Conclusion: Wholesomeness of Kent mangoes not adversely affected by irradiation to 0.75 kGy

Chinese Feeding Studies Using Human Volunteers[1]

- Eight well controlled experiments involving human volunteers consuming irradiated foods for 7 to 15 weeks
- There were 17 to 70 test subjects in each experiment, and the total number of the subjects was 439
- Each clinical test in all the experiments failed to find any significant difference between the control groups and the test groups consuming irradiated foods
- Seven of the eight experiments involved investigations of chromosomal aberrations in a total of 382 individuals. Some of these experiments included freshly irradiated wheat in the diet
- No significant difference between the number of chromosomal aberrations in the control groups and the test groups could be found in any of the seven experiments, either when evaluated individually or when all seven were pooled together

Potential Concerns Associated with Irradiated Foods (contd)

1. Induced radioactivity
2. Microbiological safety
3. Nutritional loss
4. Toxicological safety
5. Miscellaneous

5. Miscellaneous Concerns and Evaluations

(i) Enhanced Toxicity of Irradiated Pesticide Residues

- Regulatory limits permit only very low levels in food (say ppm)
- Any radiolytic product would be present at ppt or at worse ppb levels
- Hazard increment arising from such low levels of radiolytic products would be very small indeed

(ii) Packaging Materials Incompatible With Irradiation (Toxicological Implications)

- Packaging materials must be approved by regulatory agencies. Such approval is only granted on demonstration of safety under the proposed conditions of use

Miscellaneous Concerns and Evaluations (contd)

(iii) Undetected Failure of Treatment (since there are no sensory indicators that tell one whether or not a product was treated)

- Failure probability extremely low in properly regulated facility
- Such facilities should have quality assurance procedures in place

(iv) Regulatory Difficulties Due to the Inability to Determine Whether or Not Food Had Been Irradiated and to What Dose

- Strict requirements with respect to documentation and record keeping
- There are now some promising methods for detection of irradiated foods
- Irradiation is self-limiting technology, one cannot over-irradiate food because the sensory properties will deteriorate

In Conclusion

- Technically the advantages and safety of food irradiation have been established
- The process is being used commercially in many countries for a number of food items
- Further growth of this technology would depend upon local need and public awareness of its benefits