Skin aging and hair graying in Hiroshima

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The late consequences of irradiation—including a possible acceleration in aging—are obviously important in the present atomic era. At Hiroshima, Japan, the ages of irradiated and nonirradiated subjects were estimated on the basis of appearance, skin elasticity and looseness, and graying of hair. Results of this study refute the concept that general, nonspecific aging is accelerated as a late consequence of irradiation.

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■ Changes inherent in skin aging provide the major indexes by which chronologic age is commonly estimated, although hair graying and postural changes enter into the total impression of age. Pathologically, loss of subcutaneous fat, accompanied by decrease in skin elasticity, provide most of the basis for skin change with age.[1] More subtle changes in vascularity and skin color contribute to loss of the fresh appearance that characterizes the very young.

Investigators at the Atomic Bomb Casualty Commission (ABCC), where the delayed consequences of the 1945 atomic bombings of Hiroshima and Nagasaki are being studied, have a particular interest in aging. In many experiments in rodents, irradiation has produced shortening of the life span. It was thought that such life shortening resulted not only from the induction of specific diseases by irradiation but also from a nonspecific aging acceleration.[2,3] Warren[4] postulated the existence of a life-shortening effect on American radiologists, but subsequent, more refined statistic analysis of his data negates this finding.[5]

The possibility that irradiation accelerates aging deserves further investigation. Such investigation is especially merited among survivors of the atomic bombings of Japan, since this population is much the largest group of human beings to have received large quantities of essentially total body irradiation. Therefore, a number of physiologic investigations of aging were undertaken and a life-span study was initiated.

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Hair graying is particularly interesting as a late radiation sequela because of the sensitivity found in the melanin-producing cells of the hair follicles in irradiated rodents[6]—a sensitivity, however, which has not been noted in human beings receiving therapeutic irradiation to the head. After the atomic bombings, many of the most severely irradiated survivors experienced various degrees of temporary epilation because of damage to the hair follicle cells. That subtle permanent damage to the hair might result is a reasonable postulation. Such damage might be manifested by accelerated hair graying unrelated to general aging acceleration. Since increased hair pigmentation sometimes has been noted in therapeutic irradiation in human beings,[6] damage might even be evident through an increase in age at the onset of hair graying.

Both skin aging and hair graying are amenable to certain simple, semiquantitative estimates that can be carried out during a clinical examination. Several tests were performed on a sample of irradiated and nonirradiated subjects undergoing examination at ABCC in Hiroshima. The findings have been analyzed in relation to radiation exposure.

Methods

Composition of the sample. The measurements were carried out during standard clinical examinations on radiation exposed and nonexposed subjects who are voluntarily participating in the continuing adult health study at ABCC in Hiroshima. The sample consisted of 4 different "exposure" categories:

Group 1 consisted of proximally exposed persons, less than 2,000 meters from the bomb hypocenter, who had experienced acute major radiation damage in 1945. This damage had been manifested by epilation, purpura, or oropharyngeal complaints suggestive of agranulocytosis.

Group 2 was made up of proximally exposed persons, under 2,000 meters from the hypocenter, who had not experienced symptoms indicative of major radiation damage.

Group 3 was composed of distally exposed persons, between 3,000 and 3,500 meters from the hypocenter, who were beyond the area of radiation but within the area of blast and other damage from the bomb.

Group 4 comprised nonexposed immigrants who had entered the city from 1945 to 1950.

In essence, then, the 4 groups represented: (1) the most heavily irradiated, (2) the moderately irradiated, (3) intrinsic controls, and (4) extrinsic controls.

The 4 groups were carefully matched as to age and sex composition, and representative subsamples of the total were brought to the clinic monthly over a twenty-four-month cycle. This mechanism assured that a study conducted on a few hundred subjects would be generally representative of the whole sample in regard to age, sex, and exposure group. Figure I represents the age and sex composition of the entire adult health study sample in Hiroshima. Unusual features of its composition reflect the fact that many children had been evacuated from the city at the time of the bombing and that many young men were away from the city serving in the armed forces.

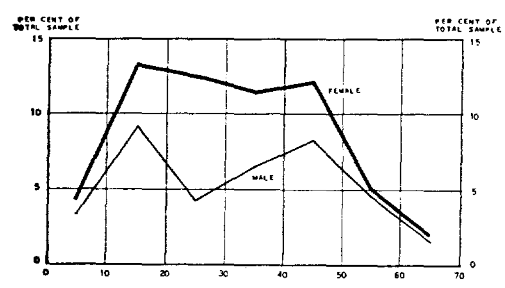

FIG. I. *Age and sex composition of entire adult health study sample in Hiroshima.*

TABLE 1 **Differences Between Nurse's Estimates and Chronologic Age**
(by Sex and Exposure Group)

Sex	Group 1	Group 2	Group 3	Group 4	Total
			Mean differences in age		
Male	−.803	−.776	−1.091	−.182	−.701
Female	+.280	+.163	+.035	+.183	+.165
			Number of cases		
Male	122	98	110	121	451
Female	232	208	227	186	853

The various tests were performed on elements of this sample, which comprised hundreds of consecutive subjects who were examined during a period of several months.

Estimate of age. One nurse, by a simple inspection of the subjects as they entered the clinic, recorded her estimate of each subject's age for comparison with actual chronologic age (table 1).

Skin retractility, skin fold size, and skin looseness. These estimates were in most instances made by the same nurse, who used a simple multipurpose spring pincer-caliper designed by one of the authors (R. A. Conard). This instrument had previously been used in studies of aging on a group of Marshall Island natives exposed to fallout from a Bikini bomb test in 1954.[7,8] The device is illustrated in figure II. Observations were made on 609 patients—their ages, sex, and exposure-group distribution are shown in table 2.

The skin retractility test simply measures the time required for a standard "pinch" to retract. Skin at the base of the right thumb, just lateral to the anatomic snuffbox, was caught in a 1-cm. opening of the pincer for a period of one minute. The time in seconds required for the skin to retract fully after release of the pincer was recorded.

The skin fold under the chin was measured for thickness. The patient sat erect, the pincer was opened to 2 cm., and the two hands of the pincer were fitted firmly to the undersurface of the mandible. The pincer was allowed to close, and the length of the skin fold caught in the pincer was recorded from the calibrations on the side of the pincer arms. In the studies on the Marshallese people,[7] skin retractility was measured several centimeters above the knuckles on the back of the hands. Skin fold measurements were done at the junction of the neck and chin; graying of the hair was measured on a 0-4+ scale.

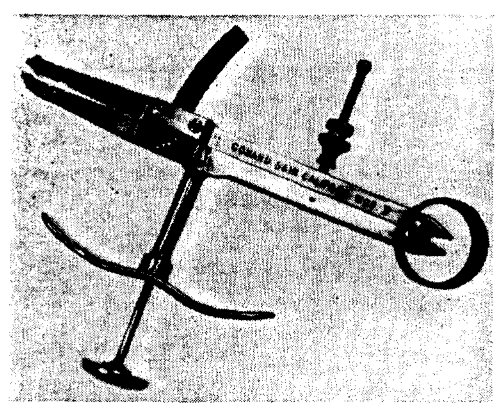

FIG. II. *Multipurpose spring pincer-caliper used for skin retractility, skin fold size, and skin looseness tests.*

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TABLE 2 **Distribution of Sample for Skin Observations**
(by Age, Sex, and Exposure Group)

Age at examination	Group 1		Group 2		Group 3		Group 4	
	Male	Female	Male	Female	Male	Female	Male	Female
10-19	5	8	3	4	1	1	4	5
20-29	7	7	6	11	11	15	7	5
30-39	9	21	10	43	8	36	7	24
40-49	11	18	7	18	7	23	11	22
50-59	11	26	11	19	4	19	11	20
60-69	5	9	14	10	10	14	7	16
70-79	2	2	1	3	4	4	1	2
80-89	—	3	—	3	—	—	1	2
Total	50	94	52	111	45	112	49	96

Skin looseness was determined by whether or not the opened pincer could pick up and hold a fold on the skin of the forearm. The pincer was opened to 2 cm. The 2 hands of the pincer were placed with moderate firmness on the undersurface of the right forearm at a right angle to the longitudinal axis of the arm and about 2 in. below the elbow. The pincer hands were allowed to spring shut, and the nurse recorded whether a fold of skin was caught by the maneuver. This was simply a negative or positive test without quantitation of the size of the skin fold caught (table 3).

Hair graying. Hair graying in the temple area was estimated by a simple scoring system that utilized a 0 to 3+

TABLE 3 **Percentage of Patients Whose Skin Folds Were Caught**
(by Age and Exposure Group)

Age at examination	Group 1	Group 2	Group 3	Group 4	Mean total percentage
10-19	61.5	57	50	44	55
20-29	64	76.6	84.6	83.5	78.5
30-39	96.5	98	100	97	97.5
40-49	100	100	100	100	100
50-59	100	100	100	100	100
60-69	100	100	100	100	100
70-79	100	100	100	100	100
80-89	100	100	100	100	100

scale. While the subject was lying down for his routine electrocardiogram, the nurse inspected the temple areas for gray hairs. The choice of site and the scoring method were based on the findings of Terada,[9] who studied hair graying in Japanese subjects very carefully with more quantitative methods. In the scoring system, 0 = no gray hair; + = few grey hairs; ++ = moderate gray hairs, and +++ = almost completely gray.

Results

Estimate of age. The nurse's observation simply provided an estimated age of the subject—based on physical appearance—for comparison with his actual chronologic age. The subjects came through the clinic, of course, without the observer knowing their exposure histories.

Ages of 1,304 subjects were estimated. The size of the sample according to exposure group and the mean differences between estimated and actual ages are shown in table 1. It can be seen that the nurse systematically overestimated the age of male subjects, and only slightly underestimated the age of females. Estimates were more exact for females; 95 per cent confidence limits on the difference (actual—estimated) were —4.7 to +5.1 years for females and —7.2 to +5.8 for males. These individual differences were too slight to affect the validity of the comparisons of the radiation exposure groups.

The relationship to exposure status was studied by comparing the mean differences for exposure groups. Also studied was a regression analysis of the age differences and distance of survivors from the hypocenter (combining both groups 1 and 2). The differences noted in both analyses were well within the usual range of chance variation, so that

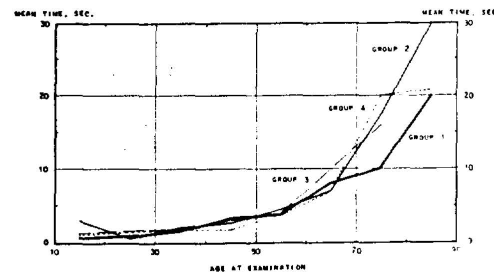

FIG. III. *Mean time for skin to flatten completely, by age and exposure group.*

it could not be concluded from these data that the irradiated subjects looked any older than the nonirradiated subjects.

Skin retractility. This determination was performed on 196 males and 413 females—a total of 609. The test measured the time in seconds required for a standard "pinch" to flatten completely. The test showed good correlation with age, but differences were more marked in the older age group. The correlation ratio was .66 for the total sample, which indicates that approximately 43 per cent of the total variation was accounted for by age alone.

Since no sex differences were detected, both sexes were combined for exposure group comparisons. Figure III shows the mean retractility time of the 4 exposure groups. It is evident that the exposure groups were quite homogeneous. An analysis of variance failed to suggest any relationship between skin retractility and irradiation.

Skin looseness. This test proved of relatively little value except in the younger age groups. During spring-release closure, the pincers were able to catch a skin fold on the forearm in virtually 100 per cent of subjects beyond the age of 30. Table 3 shows the percentages by age and exposure group for both sexes combined. Again, no relationship to radiation exposure was detected in this technically unsatisfactory test.

TABLE **4**

Mean Length of Neck Fold in Millimeters
(by Age, Sex*, and Exposure Group)
and Standard Deviation
(by Age)

Age at examination	Group 1			Group 2			Group 3			Group 4			Total			
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	S.D.
10-19	3.0	3.2	3.2	3.7	5.0	4.4	6.0	6.0	6.0	1.2	4.0	2.8	2.8	4.0	3.5	2.49
20-29	4.3	5.3	4.8	5.8	6.0	5.9	5.8	5.4	5.6	5.9	6.0	5.9	5.5	5.6	5.6	1.13
30-39	6.7	6.4	6.5	5.6	6.2	6.1	6.0	6.5	6.4	5.9	6.5	6.3	6.0	6.4	6.3	0.95
40-49	7.4	6.7	6.9	7.1	6.9	7.0	6.7	6.9	6.8	6.5	6.9	6.8	6.9	6.8	6.9	0.94
50-59	7.5	7.3	7.4	7.7	7.2	7.4	6.0	7.5	7.2	7.3	7.2	7.3	7.3	7.3	7.3	0.99
60-69	8.0	7.8	7.9	8.3	7.6	8.0	7.9	7.6	7.8	7.9	7.8	7.8	8.1	7.7	7.8	1.00
70-79	9.0	8.0	8.5	9.0	8.3	8.5	9.5	8.8	9.1	10.0	9.0	9.3	9.4	8.5	8.9	1.10
80-89	—	9.0	9.0	—	10.0	10.0	—	—	—	11.0	10.5	10.7	11.0	9.8	9.9	1.76
Mean total (all ages)													**6.7**	**6.8**	**6.7**	

*Shown as M (male), F (female) and T (total).

Skin fold length. The length of the skin fold expressed between the 2 arms of the pincers was estimated in millimeters. This estimate is related to skin elasticity; it is also related to the subcutaneous fat in the submental region, since the fat supports the skin. As the subcutaneous fat and skin elasticity decrease with age, the length of the skin fold increases. This phenomenon is manifested by the "turkey gobbler" appearance of some very old individuals.

The test was performed on 609 individuals. Rather surprisingly, no differences were found by sex. The data were clearly age-related, with age accounting for approximately 50 per cent of the total variation. The data were somewhat more variable in the younger age groups. Table 4 shows the mean length of the skin fold of the total sample in relationship to age and sex and the standard deviation of each age group. Sex and exposure groups were combined.

The data were subjected to analyses similar to those used in the skin retractility test. Findings were negative in regard to radiation.

Hair graying. The data on hair graying are considerably more complex, since they represent not only the incidence of gray hair but also a crude estimate of the degree of graying. A truly quantitative gray hair count of the type done by Terada[9] would have been highly desirable for statistic analysis but was not practical. The crude grading from 0 to 3+ added considerably more information than a simple observation of the presence or absence of gray hair could have given, but it did present problems in analysis. The data on 1,242 subjects are presented in detail in table 5; they show that the graying system detected progressive graying with advancing years. The relative deficit in younger female subjects graded as + (few gray hairs) may be an artifact of collection or may represent plucking of a few gray hairs. The latter is a relatively common practice among Japanese women. The fact that this deficit was noted mostly in

TABLE 5 **Gray Hair Observations and Age at Examination**
(by Sex, Exposure Group)

Age at examination	Group 1					Group 2					Group 3					Group 4				
	0	+	++	+++	Total	0	+	++	+++	Total	0	+	++	+++	Total	0	+	++	+++	Total
	Male																			
15-19	2				2	13				13	4				4	13				13
20-24	5				5	9				9	7				7	5				5
25-29	8				8	17				17	11				11	8	1			9
30-34	11	2			13	12				12	9				9	12				12
35-39	6				6	4				4	2	1			3	3	1			4
40-44	4	4			8	4	2	1		7	5	3			8	11	2			13
45-49	4	5	2		11	4	3	1		8	5	2			7	5	6			11
50-54	3	3	2	1	9	2	10	6	1	19	5	4	2		11	1	6		2	9
55-59	1	3	4		8	2	7	7	2	18	3	5	4		12	1	1	6		8
60-64	1	7	8	1	17		6	4	3	13		3	5	2	10	1	7	3	1	12
65-69		1	5	1	7		3	4	1	8		2	6		8	1	2	2	2	7
70-74		2	1		3		1	5	2	8		1	3		4			1	1	2
75+			1	1	2			3	1	4			1	3	4				1	1
Total	45	27	23	4	99	67	32	31	10	140	51	21	21	5	98	61	26	12	7	106
	Female																			
15-19	8				8	16				16	10				10	9				9
20-24	5				5	19				19	16				16	6				6
25-29	16				16	12				12	8				8	8				8
30-34	33				33	28				28	10		1		11	20		1		21
35-39	18		1		19	28				28	15				15	11		1		12
40-44	14	2	1		17	29	5			34	14	7	1		22	10		1		11
45-49	13	6	2		21	23	7	3		33	12	8	2		22	9	6	1		16
50-54	9	6	6	1	22	18	10	9		37	8	5	6		19	4	3	3	1	11
55-59	4	6	13	1	24	9	11	9	2	31	2	3	6		11	7	7	7		21
60-64	1	5	8		14		12	10	3	25		2	10	4	16		7	7	1	15
65-69	1	2	7	1	11	2	3	6		11		4	8	2	14		1	2	1	4
70-74	1		5	2	8		3	4	3	10			4	1	5		1	1	1	3
75+			1	1	2			1	2	3		1	1		2			3	1	4
Total	123	27	44	6	200	184	51	42	10	287	95	30	39	7	171	84	25	27	5	141

TABLE 6 **Estimated Mean and Standard Deviation for Age at Onset of Gray Hair**
(by Sex and Exposure Group)

Exposure group	Male		Female	
	Mean	Standard deviation	Mean	Standard deviation
1	45.5	10.6	50.0	9.5
2	46.4	6.2	51.0	6.0
3	48.8	8.0	49.5	9.0
4	47.0	11.1	50.5	7.0

the female groups suggests that hair plucking was the cause.

Analysis of simple incidence of gray hair in the population discloses a sigmoid curve characteristic of a normally distributed variable. By means of probit analysis,[10] the mean and standard deviation was estimated for age of the population at onset of gray hair (table 6). It can be seen that women begin to gray somewhat later than men. This difference might be related to the common practice of hair dyeing among Japanese women. However, the hair roots were closely inspected during data collection, so that this probably represents a true sex difference. Comparison of the means for the 4 exposure groups was generally negative, except that the means for men differed by a suggestive amount (P was between .05 and .10). This was largely the result of the high mean age of onset of gray hair in the distally exposed group 3. Comparison of the heavily exposed group 1 with the extrinsic control group 4 showed no significant difference in mean age at onset of gray hair ($P = .2$).

Regression analysis of the gradations of hair graying was undertaken, with the ratings 0 to 3+ being replaced by the numbers 0, 1, 2, and 3. The fit was reasonably satisfactory for most age groups, and the slopes of the regression lines did not differ significantly. The slopes and the corresponding correlation coefficients are shown in table 7. Although the slopes of regression are similar in men and women, the age for women is shifted to the right. This again indicates that Japanese women become

TABLE 7 **Slopes of Regression Lines and Linear Correlation Coefficients for Arbitrary Graying Score in Relation to Age**
(by Sex and Exposure Group)

Group	Slopes of regression lines		Correlation coefficients	
	Male	Female	Male	Female
1	.235	.284	.738	.720
2	.273	.317	.785	.678
3	.290	.275	.788	.735
4	.270	.240	.719	.689

gray somewhat later than men.

To study the radiation effect more effectively with these data, measures of radiation dose and hair-graying that can be applied to the individual case were used. Distance from the hypocenter was used as an approximation for radiation exposure. To measure hair-graying, departure from the norm was used; that is, the amount an individual's score varied from the regression value typical of his age and sex.

The method in this analysis was to use the regression estimate to define an age-specific measure of grayness as : $Z = Y' - Y$. Y' is the regression estimate for specified age and sex based on the nonexposed, Y is the numerical value for the individual (0, 1, 2, or 3), and Z is the measure of the individual's departure from expectation for his age-sex group.

Mean values of Z were tested for departure from zero. If, for any sex-exposure group, individuals were more, or less, gray than expected from the regression estimates, the mean value of Z for that exposure group would depart from zero and the departure would be tested by Student's t-test.

If high exposure (short distance) was accompanied by large negative values of Z, and low exposure (long distance) by values of Z near zero, the relationship would be tested on the correlation coefficients or on the slopes of regression lines fitted to Z and distance. None of these analyses provided evidence that hair-graying is related to distance from the hypocenter.

Discussion

In this study, several simple tests were utilized in an attempt to detect skin changes in irradiated survivors of the Hiroshima bombing; changes that would be indicative of generalized aging acceleration as a late radiation sequela. The most direct test was guessing the age of clinic subjects without knowledge of their irradiation status. This very simple observation may have been the most important, since it established the fact that irradiated individuals do not appear older than their nonirradiated cohorts.

The pathologic components of skin ageing are mostly related to degeneration of skin elastic fibers and to loss of subcutaneous fat. Skin retractility was measured as a direct reflection of elastic tissue in the skin. A skin fold measurement (essentially wrinkling) was more directly related to loss of subcutaneous fat, although loss of elasticity did play a role. The methods of skin measurement employed were not as elaborate and were perhaps less sensitive than those employed by other investigators.[11] However, the methods used lent themselves better to large population surveys. In spite of the moderately large samples used in this study, no relationship to radiation exposure and skin aging was noted.

Hair graying is of particular interest, not only as a manifestation of aging, but also as it relates to the epilation experienced by heavily irradiated subjects in 1945. Data on the age incidence of gray hair, as well as the semiquantitative grading of degree of graying, failed to show differences between the exposed and nonexposed. This was true even though epilation subsequent to the bombing was a common symptom of the most closely exposed group in the sample.

The concept of nonspecific shortening of the life span after irradiation has been based primarily on experiments in rodents. This concept is that decreased longevity results from irradiation, and that this decrease is not related to life-shortening diseases specifically induced by irradiation. In these experiments on rodents, specific metabolic or endocrine disturbances have not been searched for, and, in many experiments, the pathologic findings have not been carefully enumerated. Recent studies have questioned the validity of the concept of nonspecific shortening of the life span.[12,13]

There are no data on human beings that support the concept of nonspecific aging acceleration as a late consequence of irradiation. The studies reported here concern certain aspects of aging of skin and hair in a Hiroshima population. These studies fail to show any evidence of a generalized aging acceleration resulting from the 1945 atomic bombing. The validity of the concept of aging acceleration in human beings as a late consequence of irradiation is of obvious importance in this burgeoning atomic era. At the Atomic Bomb Casualty Commission, many different age-dependent physiologic processes are being studied to gain more information on this largest group of heavily irradiated people.

Summary

Estimation of age by appearance, skin elasticity and looseness, and hair graying were studied in the irradiated and nonirradiated population of Hiroshima. No differences in these several measurements were detected between the radiation-exposed and nonexposed components of the sample. The study provided no support for the concept of a general, nonspecific aging acceleration—exemplified by aging of skin and hair—as a late radiation sequela.

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