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AN ATTEMPT TO QUANTIFY SOME CLINICAL CRITERIA OF AGING*

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Among the possible late effects of ionizing radiation exposure are shortening of life span and a process resembling premature aging. In animals these effects are evidenced by such changes as graying of the hair (7), appearance of degenerative changes in tissues and organs (1, 2), and deaths associated with degenerative diseases and malignancies (6). Although evidence for premature aging *per se* has not been observed in human beings, shortening of life span and increased incidence of malignancies have been reported in radiologists (10, 11). Japanese exposed to nuclear bombings have shown an increased incidence of leukemia (9). Another human population which received significant radiation exposure are the people of Rongelap Atoll in the Marshall Islands, who were accidentally exposed to fallout in 1954. In view of possible effects of radiation in producing premature aging, during the course of studies of these people it was desirable to develop a method of measurement of aging. It seems pertinent first to briefly summarize the radiation effects in the Rongelap people, since they were the subject of this study.

A group of 64 Rongelap people received an estimated 175 r of gamma radiation in addition to beta burns of the skin and some internal absorption of radionuclides. Also 18 other Rongelapese who, by virtue of being away on a nearby island, received only an estimated 69 r. Due to radioactive contamination of their home island, the people of Rongelap were moved to Majuro Atoll where they lived for the following three years. They returned to Rongelap in the summer of 1957 accompanied by some 100 unexposed Marshallese relatives who had not been living on the island at the time of the accident. This group served as an excellent comparison population. Both groups have been carefully studied at intervals for signs of radiation effects. The acute damage (such as hemopoetic depression, and skin burns) which have been described in previous publications (3, 4, 5) has largely subsided, and greater emphasis is now being placed on detection of late effects of radiation. Shortening of life span has not been apparent thus far. Four deaths have occurred: one in a 46-year-old man during the second year after exposure from hypertensive heart disease, which had been present at the time of exposure; the second in a 76-year-old man at three years post-exposure of coronary heart disease complicating diabetes of long standing; the third in a 36-year-old man 4 years after exposure with acute varicella; and the fourth in a 61-year-old female at 5 years after exposure of ovarian cancer. None of these deaths seemed to be directly related to radiation effect, and the incidence of mortality is about the same as for the Marshall Islands as a whole. No case of leukemia or cancer, except the one case of cancer referred to above, have occurred. The incidence of degenerative diseases seems to be about the same in the exposed as in the unexposed group. Reproductive capacity does not seem to have been impaired in the exposed group. A slight increase in the number of miscarriages and stillbirths seems to have taken place in the exposed women but, due to lack of vital statistics, this cannot be properly evaluated. There also was suggestive evidence of a slight lag in growth and development of exposed children during the first few years post-exposure, but this is being re-evaluated based on better age data. No genetic effects have been observed in the children born of exposed parents.

Although there has been no outward evidence by gross observation of any accelerated aging effect of radiation on the exposed group, it was believed that it would be desirable to have measured criteria of possible age changes that might occur on normal physical examination. Therefore the over-all objective of this study was to establish a series of tests to evaluate any possible radiation-induced senescence in the exposed group compared with the unexposed population living on the same island. However, a study of the data to be presented that was collected during the past survey (March, 1959) 5 years after exposure showed no apparent differences between the exposed and unexposed groups. Therefore the two groups have been pooled with the objective of

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presenting the methodology of approach, the trend of changes for the various aging criteria chosen, and an attempt to determine a biological age score for the individuals and different age groups.

MATERIALS AND METHODS

This study was hampered by the small number of people involved and the lack of vital statistics on the Marshallese people. Another difficulty has been the uncertainty of exact ages in some cases, particularly in older people.

The aging criteria to be presented were recorded only in adults, that is in those 20 years of age and over. Data were recorded on 126 adults, 42 in the originally exposed group and 84 in the larger comparison population. Table 1 shows age and sex distribution of the people

TABLE 1. RONGELAP ADULT POPULATION AGE DISTRIBUTION (1959).

Age	Exposed		Unexposed		Total
	M	*F*	*M*	*F*	
20 - 24	0	5	1	6	12
25 - 29	2	1	12	6	21
30 - 34	3	2	3	5	13
35 - 39	1	4	4	4	13
40 - 44	4	2	6	3	15
45 - 49	1	0	2	3	6
50 - 54	1	0	5	5	11
55 - 59	2	1	3	1	7
60 - 64	0	5	5	3	14
65 - 69	0	0	2	3	5
70 - 74	1	2	0	0	3
75 - 79	0	1	0	0	1
>80	2	1	2	0	5
					126

examined. The ages were reasonably well distributed except for a smaller number of older people (> 60 years of age).

The age criteria chosen were based on changes generally believed to be associated with physiological senescence and represent only a small number of those that might have been considered. They were selected, however, with a view toward ease of assessment during routine physical examination under field conditions, time limitations, and language barrier. Therefore, unfortunately, tests of vigor and functional capacity were necessarily limited.*

There were 15 tests selected, 9 of which were measured directly and 6 of which were estimated on a 0 through 4− scale. There were 5 tests involving the integument: 1) skin looseness, 2) skin elasticity (retraction time), 3) senile changes in the skin, 4) graying of the hair, and 5) baldness. There were four tests involving the special sense organs: 1) accommodation, 2) visual acuity, 3) arcus senilis, and 4) hearing. The cardiovascular system was tested by: 1) systolic and diastolic blood pressure recordings, 2) peripheral arteriosclerosis, and 3) retinal arteriosclerosis. There was one test of neuromuscular function. Vigor was measured by hand strength measurements. The methods used in carrying out these tests follow.

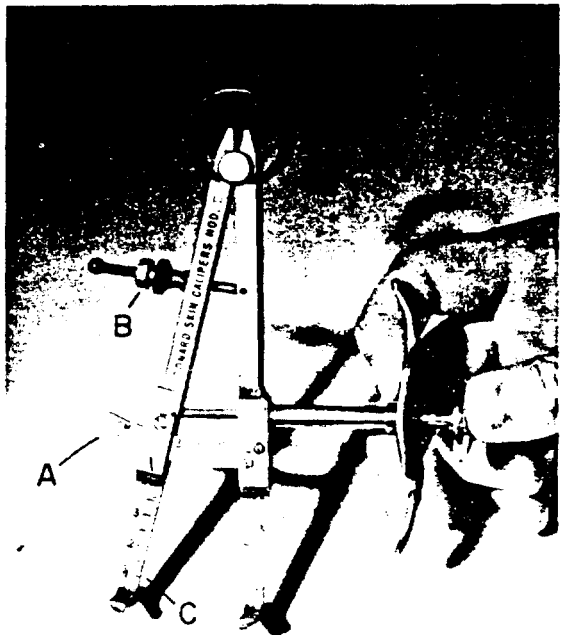


Fig. 1. Calipers used for measurement of skin looseness and elasticity.

Integument: A special skin caliper was designed for measuring skin looseness and elasticity. (See fig. 1.) The legs of the caliper can be opened to any desired degree to as much as 5 cm. (on scale "A" by adjusting screw "B" in fig. 1). The spring tension when the caliper is closed on a fold of skin results in a pressure of about 500 Gm. The inner and outer surfaces of the legs of the calipers are calibrated in millimeter markings ("C" in fig. 1).

1. *Skin looseness.*—Preliminary investigation revealed that the skin fold at the junction of the chin and neck was the most satisfactory for the measurement of skin looseness and seemed to be best correlated with age. The measure-

* There were several tests such as pulse-blood pressure response to a two-step test and vital capacity that were tried out but not used since they proved unsatisfactory.

ment of skin looseness was carried out by grasping the skin with the thumb and forefinger, pulling it gently outward, and applying the caliper opened to 4 cm. so that each leg was firmly against the skin lateral to the fingers. The caliper was then allowed to close by its own spring tension and the height of the fold of skin impinged was measured in millimeters on the scale "C" of the caliper. The elongated ends of the legs impinge on 1 cm.^{2} surface of skin and exert a pressure of 500 Gm. There is little variation in spring tension in the last 2 cm. closing range of the caliper. The height of the fold represented the degree of skin looseness. The presence of excess fat in the skin probably made the readings err on the low side, but it was not believed this resulted in serious error.

2. *Skin retraction time.*—The state of elasticity of the skin was found to be best measured on the back of the hand. The hand and forearm were placed at rest on the table. The caliper was opened to 2 cm. (as measured on the crossarm scale) and allowed to close on a fold of skin several centimeters proximal to the knuckles near the middle of the hand so that the long axis of the fold was diagonal (45°) to the longitudinal axis of the hand. (This was done to avoid natural folds of skin.) The caliper was allowed to remain closed for exactly 60 seconds, then removed and the time for the skin fold to retract back to the normal skin contour was measured in seconds. The exact endpoint was sometimes difficult to measure in older people, and if the fold had not retracted completely in 90 seconds, this time measurement was used.

A reliability test of the skin looseness and skin retraction time was run on 20 hospital patients of various ages. Measurements taken with the skin calipers were recorded by two examiners. The following mean values with their standard deviations were obtained: for skin looseness in millimeters, 20.85 ± 0.71 and 20.90 ± 0.70; for skin retraction time in seconds, 58.2 ± 8.13 and 58.75 ± 8.18. There was no significant difference between the means of the two examiners. Prior to the test, the two examiners ascertained that their techniques for using the calipers were alike.

3. *Senile changes in the skin.*—The exposed skin of the hands and face were observed for the presence of senile changes such as keratoses, nevi, and pigmentation. The degree of such change was estimated on a 0 – 4+ scale; only an occasional abnormality was scored as 1+, more abnormalities were scored ranging up to 4+.

4. *Graying of the hair.*—The degree of graying of the hair was expressed on a 0 – 4+ scale as follows: 0, no graying; 1+, slight "salt and pepper"; 2+, moderate "salt and pepper"; 3+, nearly complete graying; and 4+, complete graying.

5. *Baldness.*—The degree of baldness was expressed on a 0 – 4+ scale as follows: 0, no apparent balding; 1+, slight receding of the hair at the temples; 2+, marked receding of the hair at the temples with some thinning; 3+, marked thinning and baldness; and 4+, baldness complete to a monk's cap type.

6. *Special senses.*—(a) *Eyes.*

(1) *Accommodation.* — Accommodation was measured in diopters by use of the Prince refracting rule.* The average reading of the two eyes was used.

(2) *Visual acuity.*—Visual acuity was measured by Snellen's test.* It was found that by taking the square root of the average visual acuity (denominator) of the two eyes the scale was more compressed and more linear. Thus the best vision of 20/10 was represented at 3.2 (the square root of 10), the worst reading of 20/200 was represented as 14.1 (the square root of 200), and intermediate readings similarly recorded.

(3) *Arcus senilis* was estimated in the 0 – 4+ scale. Only slight limbic clouding was considered 1+ with increasing clouding to marked clouding as 4+.

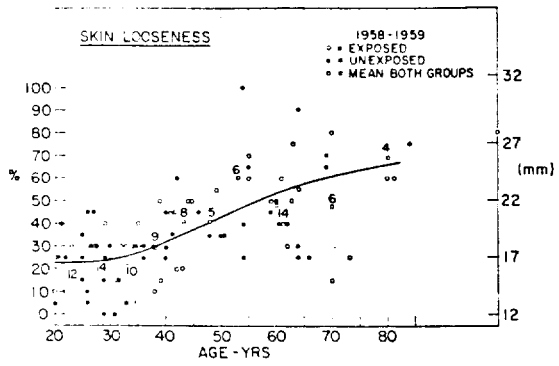
(b) *Hearing.** — Audiometric examination was carried out in a tent in a quiet location. A rugged screening type audiometer was used.† Impairment of hearing was averaged for the two ears as follows: the decibel loss for each of 7 frequencies (200, 500, 1000, 2000, 3000, 4000, 7000) in each ear was averaged and a mean frequency loss in decibels for the two ears was obtained.

Cardiovascular changes:

1. *Blood pressure.* — Systolic and diastolic blood pressures were obtained with the stand-

* With regard to the reliability of determinations using the Prince refracting rule, Snellen's test, and hearing acuity, it should be pointed out that these tests were carried out under standardized conditions, but in view of the necessity of using an interpreter under field conditions, it was not feasible to repeat the test by more than one examiner. It is believed, however, that the data from these tests were sufficiently reproducible to be of relative value, although not so accurate perhaps as might be obtained under more desirable conditions.

† The author is grateful to the Armed Services Medical Procurement Agency, Fort Totten, N. Y. for loan of the audiometer.



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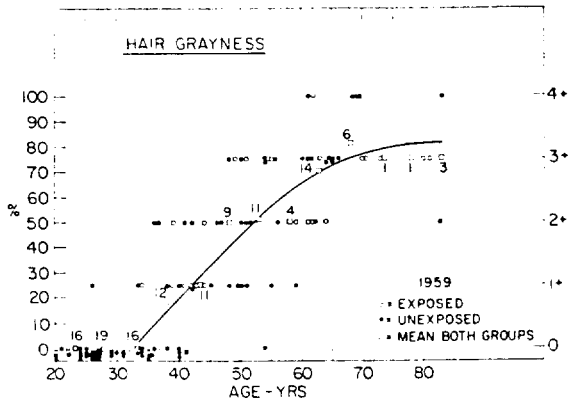

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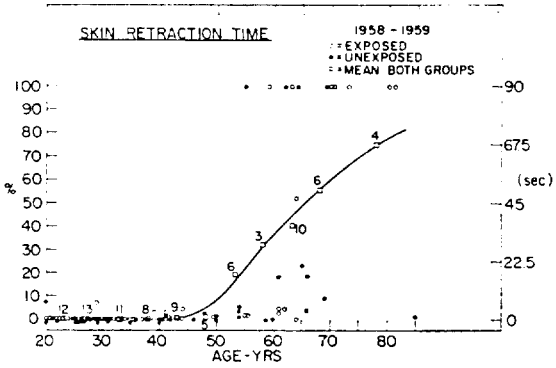

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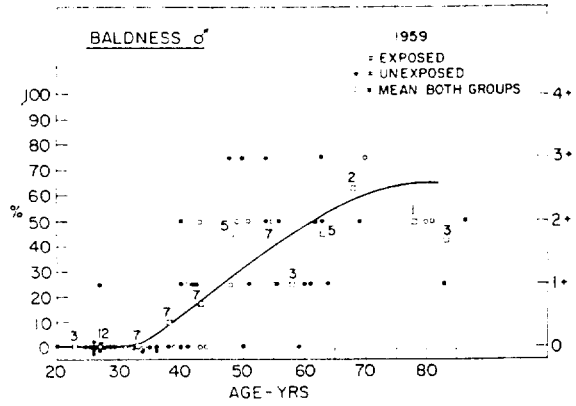

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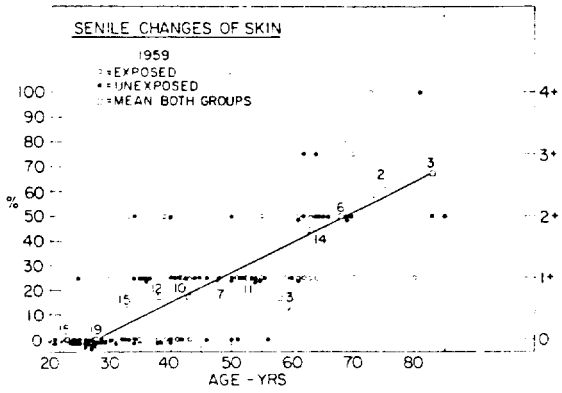

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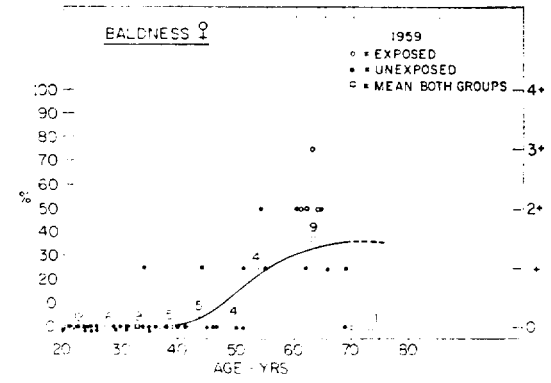
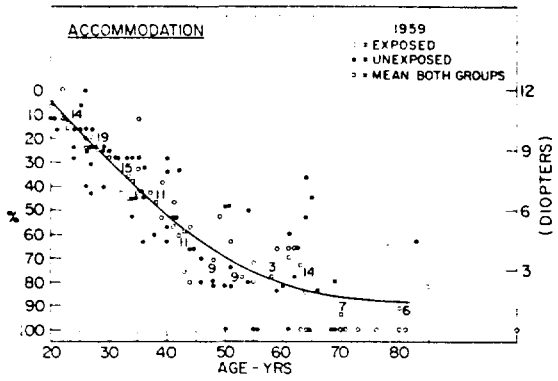


Figure 7.

ard aeronoid cuff type sphygmomanometer. Two readings were obtained and the average of the two was used. There was no basic or adjusted level of physical activity such as resting for a standard period prior to the readings. Pressures were taken from the left arm with the subject supine during the course of the physical examination.

2. The degrees of *peripheral arteriosclerosis* and *retinal arteriosclerosis* were estimated on a 0 – 4+ scale. Peripheral arteriosclerosis was estimated by palpation of peripheral arteries, retinal arteriosclerosis by viewing the retina with an opthalmoscope.

Neuromuscular function was measured by having the subject depress the key of a hand tally type of blood cell counter as many times as possible in the period of one minute. The total number of depressions represented the score.



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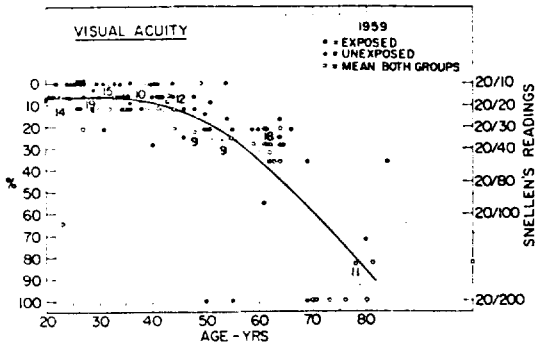

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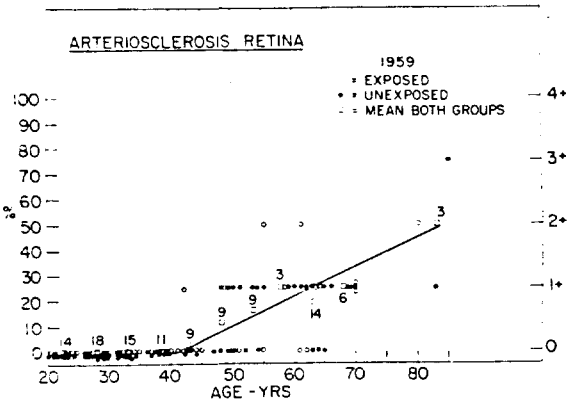

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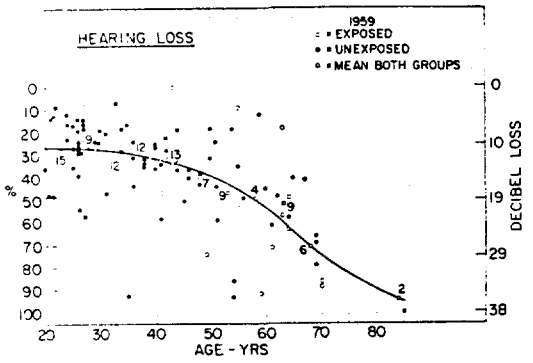

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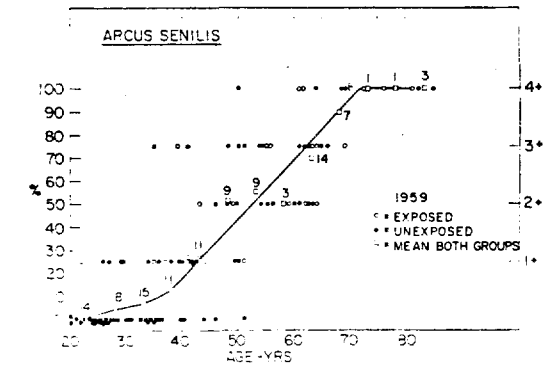

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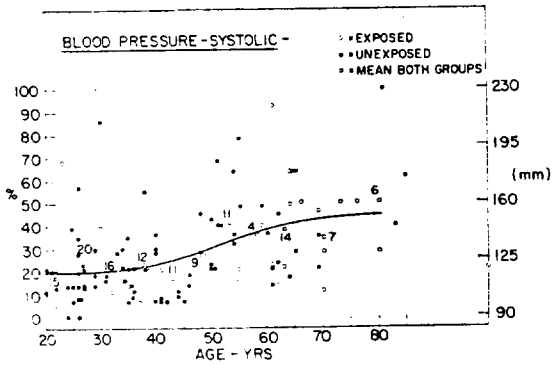


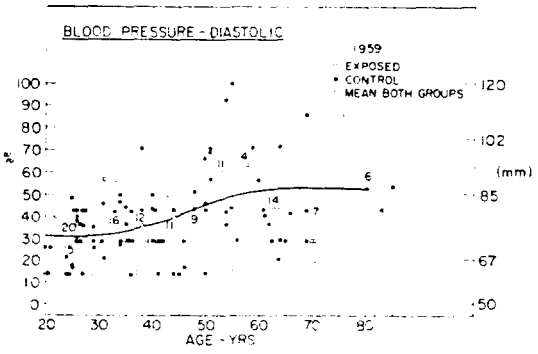
Figure 13.

Hand strength was measured by a Smedly hand dynamometer.* The spring tension of the hand grip was measured in kilograms. The maximum squeeze strength in the dominant hand in three tries was recorded.

Due to sex differences, the following criteria described above were evaluated separately for the two sexes: baldness, neuromuscular function. and hand strength.

* C. H. Stoelting Company, Chicago, Ill.

In order that the estimated and measured data could be compared and combined, both types of data were converted to a percentage scale. The estimated values of 0, 1+, 2+, 3+, and 4+ were thus presented also as 0, 25, 50, 75 and 100%, respectively. The measured data were similarly handled. Thus the values associated with least aging were chosen as 0% (sometimes the highest reading, as with hand strength; sometimes the lowest, as with hear-



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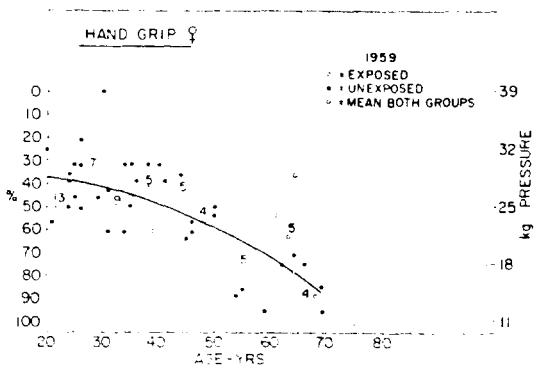

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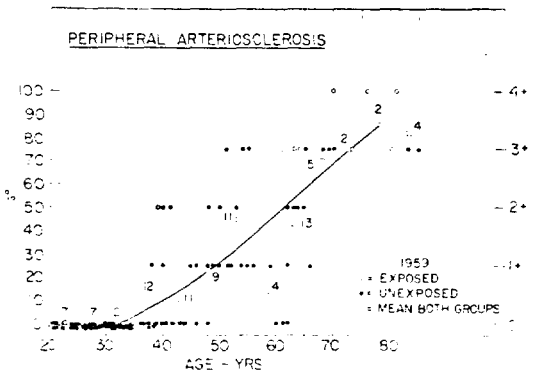

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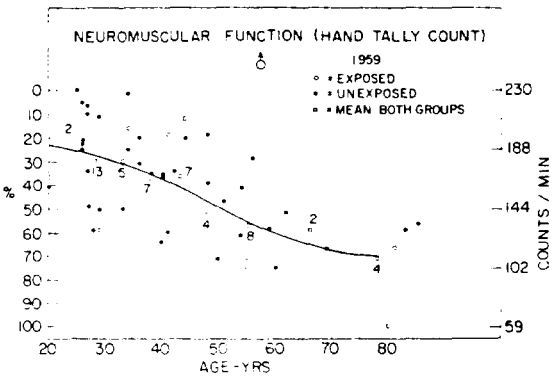

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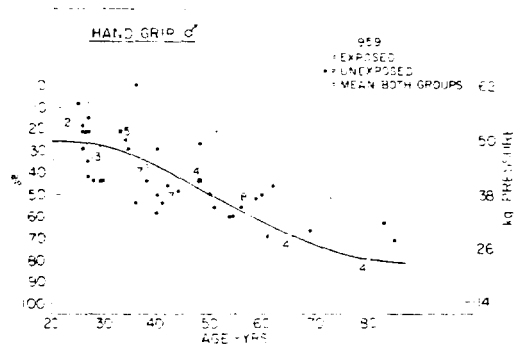

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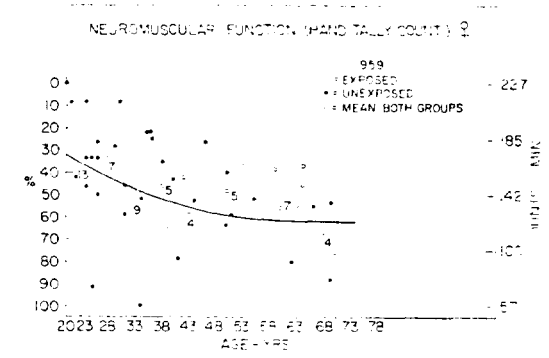

Figure 19.

ing loss), and conversely the values showing most aging were chosen as 100%. The data were examined on an individiual basis as well as on a population basis. A mean age score was obtained for each individual by averaging all the determinations in percentage for that individual. In studying population trends for the various criteria, mean points for 5-year age groups (in most cases) of combined exposed and unexposed populations were plotted and a best fit by eye curve drawn to show the trend of the data for the particular criterion. In the same way the average age scores were plotted for the population. By combining scores from individuals in each 5-year age group, it was believed that possible errors due to uncertainty of exact ages in some individuals were reduced

RESULTS

The results are plotted graphically in figures 2 through 20. Individual readings are plotted (open circles, exposed people; closed circles, unexposed people) to show the spread of the data and the mean values for each 5-year age group (squares). The trend of the various criteria with increasing age is represented by a best fit

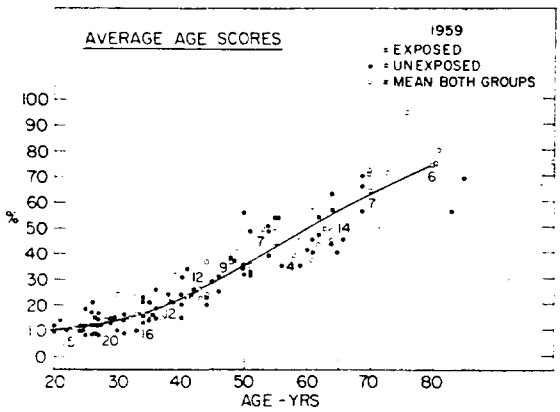

Figure 20.

by eye line. It can be seen that the criteria generally show either increasing or decreasing values with increasing age. Many of the changes, such as graying of the hair, balding, arteriosclerosis — peripheral and retinal, skin looseness, and skin retraction, do not manifest themselves appreciably until after ages 35 to 40 years in the Marshallese. There is a tendency in many of the curves for criteria, such as blood pressure, graying of the hair, and loss of visual acuity and accommodation to level off, plateau, or even show slightly reduced values in the older age group. The number of people in the older age group is too small to make this observation certain. However, American statistics on blood pressure (systolic and diastolic) do show a plateau effect beyond about 60 years of age and even a slight tendency to lowering of blood pressures beyond this age (8). By 65-70 years of age, arcus senilis in all Marshallese showed a 4+ change and so, of course, plateaued at a maximum. Some curves showed lower maximums than others. For example, baldness in women showed only 35% maximum, and arteriosclerosis of the retina showed only 45% maximum. It is likely that the difference in the maximums among the various criteria presented was due largely to differences in the degree of changes associated with the various criteria, but also probably due to the arbitrary nature of the scoring. The sex differences in hand strength and baldness were expected. In the neuromuscular function test slight muscle fatigue may have been a factor in causing the females to score lower, necessitating separate treatment.

DISCUSSION

The various changes generally associated with physiological senescence are known to show wide variability among individuals of the same age, and this was borne out by these data. However, some of the criteria seemed to be better indices of aging than others, based on the degree of change and the variability of the data observed.* Some of the better criteria seemed to be accommodation of the eyes, visual acuity, skin retraction, arcus senilis, graying of the hair, and hand strength. One would expect that the measured criteria would be more reliable than the estimated ones in view of the subjective element and less precise scoring of the latter. This seemed generally to be the case, although the estimated values for graying of the hair and arcus senilis were surprisingly well correlated with age. The amount of subcutaneous fat probably influenced the skin looseness measurements, but since loss of subcutaneous fat is somewhat age dependent, it probably influenced it in the right direction. In the future it is hoped that by statistical treatment of the data a weighting factor may be assigned to each criterion based on the degree of age-associated change and the degree of variability of the data. Since it is not always possible to run the complete battery of tests on each individual, use of such weighting factors on those tests run would tend to minimize disparity that might be related to the omission of tests that were not run.

The data presented must be considered as preliminary in nature and represent only a small fraction of the many varied changes that have been incriminated in the aging process. However, under the conditions of examinations of the Marshallese the battery of tests employed is necessarily limited. As more experience is gained, some of the tests may be eliminated and new ones added. It is believed the tests of vigor are extremely important in assessing aging and it is hoped that more tests of this nature may be added. At this time the data are presented to introduce a type of approach which might offer a feasible means of assaying biological age. Studies of the possible effects of radiation on the aging phenomenon in human beings may be aided by this method. In the case of the exposed Marshallese, results of further aging surveys will be carefully evaluated, comparing results in the exposed population with those

* Statement is not based on statistical analysis.

In the unexposed comparison population for differences which might indicate possible premature aging effects of radiation exposure. As pointed out, such differences have not been apparent thus far.

SUMMARY

In order to study possible premature aging effects of radiation in the people of Rongelap in the Marshall Islands, a series of measurable criteria generally associated with aging were recorded during the 1959 annual medical survey (5 year post-exposure) on 42 people who had been exposed to radiation and 84 unexposed Marshallese. The criteria were chosen on the basis of ease of assessment under field conditions considering time limitation and language barrier. Some criteria were assessed on observation by scoring on a 0 through 4+ and percentage basis (senile skin changes, graying of hair, baldness, arcus senilis, peripheral arteriosclerosis, retinal arteriosclerosis). The other criteria were measured directly and also expressed on a percentage basis (skin looseness, skin elasticity, accommodation of the eyes, visual acuity, hearing by audiometry, blood pressure, neuromuscular function, and hand strength). A skin caliper used for measuring skin looseness and elasticity was described. Since no differences were readily apparent between the exposed and unexposed people, the data were pooled and presented at this time to describe the methodology, trend of criteria changes with age, and attempt to assess biological age. Curves of the plotted data drawn by eye showed varying degrees of age-associated change with different criteria. The measured criteria were generally best correlated with age, particularly accommodation of the eyes, visual acuity, skin elasticity, and hand strength, although some of the observational criteria, such as arcus senilis and graying of the hair, seemed also to be fairly well correlated. A plot of the average percentage scores for individuals by age (biological age score) showed generally increasing scores with ages and less scatter than was noted with individual criteria. It is hoped that this approach may prove helpful in assessing aging in human beings and may offer a clue to possible radiation-induced aging.

The author wishes to express his gratitude to Mr. William Scott for his assistance in compiling the data; to Col. Austin Lowrey (MC) USA of Walter Reed Army Hospital, Drs. B. S. Blumberg of National Institutes of Health and W. H. Lewis of Memorial Hospital for their assistance in taking measurements on the Rongelap people.

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