EXPERIMENTAL EPIDEMIOLOGY OF TUBERCULOSIS

The Prevention of Natural Air-Borne Contagion of Tuberculosis in Rabbits by Ultraviolet Irradiation*

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It is generally believed that human pulmonary tuberculosis is acquired by the inhalation or aspiration of particles or droplets carrying tubercle bacilli. While there is no agreement as to the size of the entities involved, cogent evidence has been presented (1) which suggests that the dimension of these objects must be much smaller than the lumina of the terminal bronchioles through which, it is presumed, the infectious units must pass for the disease to take root. It was demonstrated in 1930 (2) that the incidence of respiratory tuberculosis, naturally acquired by guinea pigs placed in a room where tuberculous animals were shedding tubercle bacilli in their environment, was independent of the proximity of these animals to the sources of contagion. Apparently, therefore, the microorganism was uniformly distributed throughout the air of this room. Since it was further found (3) that pure cultures of tubercle bacilli suspended in the air could be killed by exposure to ultraviolet radiation, it became desirable to determine whether natural air-borne contagion of tuberculosis can be prevented by this means.

During the past 10 years (4) the pattern of the disease acquired by natural respiratory contagion of certain inbred rabbit families over many generations has demonstrated that our family A is genetically and uniformly highly resistant to tuberculosis. Families C and F, on the other hand, are genetically and uniformly of low resistance to the infection. In the study here reported these three families were used, first, to equalize the natural resistance of the experimental and control animals and, second, to determine whether ultraviolet radiation will have a greater protective influence on the animals of high resistance as compared with those of low resistance.

Materials and Methods

Experiment of 1941–42

The general procedures used in conducting natural respiratory contagion experiments in rabbits have been fully described (4). Briefly, rabbits of the families A, C,

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and F, which had never been in contact with tuberculosis, were placed within individual cages with wire mesh walls in front and back and with solid metal walls on the sides. These cages were placed on one side of a three-tiered manifold. Six inches behind these cages the entire manifold, in each of its three tiers, was divided by a fine wire mesh screen. Behind this screen in each tier were placed four rabbits artificially infected intravenously with highly virulent bovine type tubercle bacilli, Ravenel. These rabbits, which sooner or later shed tubercle bacilli in their urine, were allowed to run about the length of the manifold, which was bedded with peanut shells. The ventilation facilities of the manifold were constructed so that in each tier the flow of air was obligatory from the sources of contagion in the runs to the contacts in the individual cages. The manifold was in two sections, each section consisting of three runs for the sources of contagion and three tiers of five cages each for the contacts. The two sections were in the same room but separated from each other by an air-tight metal partition. There were thus 15 contacts and 12 sources of contagion in each section of the manifold. The population of the contacts and the sources of contagion were kept constant by replacing the normal or infected animals by corresponding rabbits.

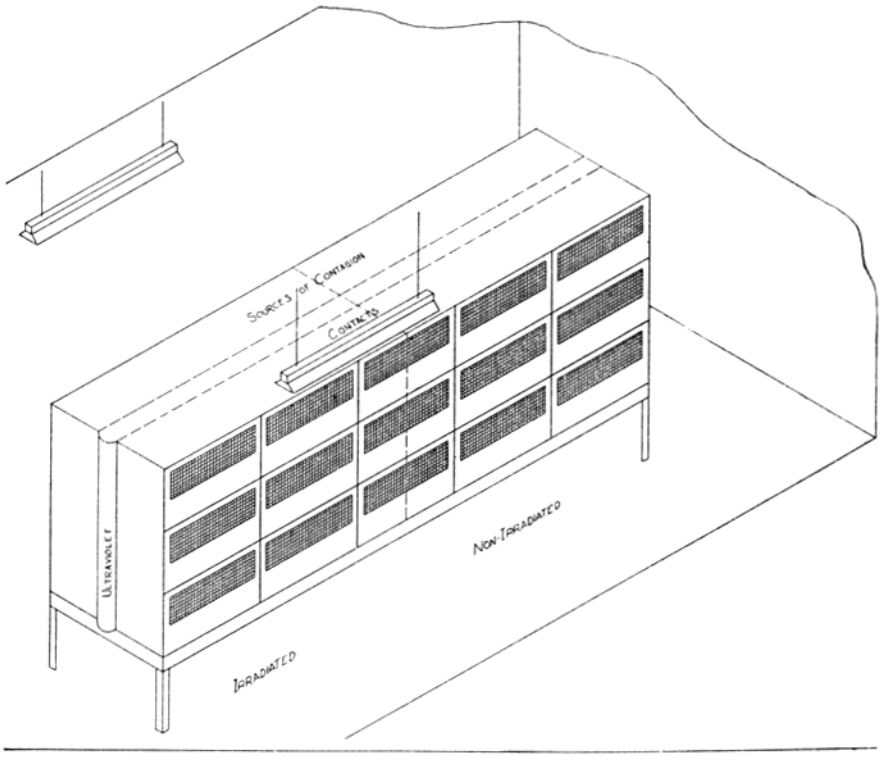
The 6 inch space between the sources of contagion and the contacts in one section of the manifold was irradiated. In the other section of this manifold this space was not irradiated. The irradiation on the experimental half of the cage was furnished by ultraviolet lamps[1] emitting monochromatic rays of 2537 Å placed vertically at one end of the barrier and reflected by a parabolic reflector to the other end of the cage, 2 meters distant (Text-fig. 1). Obviously, the intensity of radiation diminished with the distance from the source of ultraviolet energy, so that the contacts nearest the lamps were separated from the sources of contagion by a barrier of ultraviolet radiation of about 150 μw. per cm.^{2}, whereas the contacts at the opposite end of the cage were separated from the sources of contagion by a barrier of about 12 μw. per cm.^{2} (Table I). In an attempt to equalize the intensity of irradiation of the air breathed by the contacts the cages housing them were constantly rotated. As can be seen by reference to Table II, cage 15 was placed in the position of cage 1 and all remaining cages were shifted one position so that in a period of 1 month each contact was twice in an identical position in relation to the fixed source of ultraviolet energy. It can be said, therefore, that while on 2 days of each month each contact was separated from the sources of contagion by an intensity of radiation as low as 12 μw. per cm.^{2}, the average intensity of this radiation was about 40 μw. per cm.^{2}. Needless to say, the contacts in the unirradiated half of the cage were rotated in the same manner and in the same order of succession.

In addition to the irradiation of the space between the sources of contagion and the contacts within the manifold, ultraviolet lamps were also suspended horizontally from the ceiling. These were situated on both sides above the experimental half of the manifold and along its long axis (Text-fig. 1). The radiant energy of these lamps was determined from time to time by means of a modified light meter. It is to be borne in mind that the air in the control and experimental halves of the room

[1] The ultraviolet lamps in this study were kindly supplied by Dr. L. J. Buttolph of the General Electric Company.

was continuous since there was no separation between them except within the manifold itself.

Table II gives the rabbit number, the sex, age, and parentage of each of the 30 contacts on both the irradiated and unirradiated halves of the manifold. It will be seen that a member of the highly resistant family A alternated in position with a member of the family C or F of low resistance on both halves of the manifold. The digit following the letter for a given rabbit, as *e.g.* A7 = 10, indicates that this rabbit



TEXT-FIG. 1. Experiment of 1941–42.

is a member of the seventh inbred generation of the A family. It will be seen, therefore, that the genetic homogeneity of the experimental and control animals was close indeed.

In order to equalize the intensity of contagion between the experimental and control animals the four sources of contagion of each tier in the experimental and control halves of the manifold were interchanged daily so that the contacts in the irradiated section were exposed to the same infected animals as the contacts on the control side on alternate days.

Every 2 weeks all contacts on both halves of the manifold were given 0.1 cc. of

TABLE I

Intensity of Ultraviolet Energy in the Space between the Infected and Exposed Rabbits Relative to the Position of the Contact Cages in the Irradiated Half of the Manifold

Experiment of 1941–42

Cage No.	1	2	3	4	5	Ultraviolet lamp
Radiant energy, μw	16	25	50	116	—	
Cage No.	6	7	8	9	10	
Radiant energy, μw	14	22	41	103	—	
Cage No.	11	12	13	14	15	
Radiant energy, μw	6	12	21	47	146	

TABLE II

The Distribution of the Contacts in the Cages of the Manifold, Their Sex, Age in Months, and Their Parents

Experiment of 1941–42

Unirradiated section					Irradiated section				
1	2	3	4	5	1	2	3	4	5
C5-30 ♂, 6.9 C4S-26 × C4S-28 C5-47 ♂, 10.9 C4S-27 × C4S-28	A6=21 ♀, 10.6 A5=26 × A5=30	F5-14 ♂, 7.5 F4-63 × F4-48 F6-3 ♂, 16.6 F5-3 × F5-1	A7=10 ♂, 9.4 A6=5 × A5=30	C4S-30 ♀, 19.7 C3-21 × C3-18	A6=20 ♀, 10.6 A5=26 × A5=30	C5-29 ♂, 6.9 C4S-26 × C4S-28	A6=18 ♂, 16 A5=8 × A5=30	F5-15 ♂, 7.5 F4-63 × F4-48	A7=12 ♀, 8.2 A6=6 × A5=30
6	7	8	9	10	6	7	8	9	10
A7=14 ♂, 8.2 A6=6 × A5=30	C5-45 ♂, 7.6 C4S-27 × C4S-28	A7=4 9.6, ♀ A6=2 × A5=30	C5-14 ♀, 16.3 C4S-26 × C4S-20	A7=5 ♀, 9.6 A6=2 × A5=30	C5-27 ♀, 7.7 C4S-27 × C4S-28	A7=11 ♂, 8.2 A6=6 × A5=30	C5-15 ♀, 19.6 C4S-26 × C4R-20	A7=7 ♀, 9.8 A6=5 × A5=30	C5-23 ♀, 12 C4S-27 × C4R-20
11	12	13	14	15	11	12	13	14	15
F5-2 ♂, 18 F4-58 × F4-35	A7=16 ♂, 10 A6=6 × A5=30	C5-32 ♂, 6.9 C4S-26 × C4S-28	A6=11 ♂, 17.5 A5=8 × A4=20	C5-22 ♂, 12 C4S-27 × C4R-20	A7=20 ♂, 7.0 A6=6 × A6=18	F6-2 ♂, 6.0 F5-3 × F5-1	A6-2 ♂, 8 A5=26 × A5=30	C5-33 ♂, 6.9 C4S-26 × C4S-28	A6=24 ♂, 8.0 A5=26 × A5=30

1 = cage 1; C5-30 = contact of fifth inbred generation of the C family; sex; 6.9 is the age of the contact in months at the beginning of exposure. C4S-26 × C4S-28 are the parents of C5-30. In cage 1 another contact, C5-47, is recorded as it replaced C5-30 which died during the course of the experiment.

1:10 dilution of O.T. prepared from the same highly virulent bovine strain, Ravenel, as used to infect the sources of contagion. Every month the rabbits were x-rayed. In this way the origin and progress of the disease in the contacts were followed.

This experiment was conducted for 15 months. At the end of this time all surviving contacts on both irradiated and unirradiated halves of the manifold were

TABLE III

The Effect of Ultraviolet Irradiation on Natural Air-borne Contagion of Tuberculosis in Contacts of Rabbit Family A, of High Inherited Natural Resistance, and in Families C and F, of Low Inherited Natural Resistance to the Disease

Experiment of 1941–42

Rabbits exposed in unirradiated cage							Rabbits exposed in irradiated cage						
Family	Rabbit No.	Duration of exposure	No. of times tuberculin positive	Maximum tuberculin reaction of inflammation	Killed (K) or died (D)	Extent of tuberculosis at death	Family	Rabbit No.	Duration of exposure	No. of times tuberculin positive	Maximum tuberculin reaction of inflammation	Killed (K) or died (D)	Extent of tuberculosis at death
		mos.		*mm.*[2]					*mos.*		*mm.*[2]		
A	A7=16	12.9	0	—	K	0	A	A6=18	7.5	0	—	D	0
	A6=11	14.8	0	—	K	0		A7=20	11.4	0	—	K	0
	A6=21	14.8	12	1800	K	0*		A7=7	14.4	0	—	K	0
	A7=4	14.8	2	260	K	0		A6=20	14.8	0	—	K	0
	A7=5	14.8	12	3430	K	0*		A6=24	14.8	0	—	K	0
	A7=10	14.9	11	809	K	0		A6=26	14.8	1	180	K	0
	A7=14	14.9	0	—	K	0*		A7=11	14.9	2	39	K	0
								A7=12	14.9	0	—	K	0
C	C5-35	5.0	0	—	D	0	C	C5-16	5.0	0	—	D	0
	C5-30	6.3	6	1672	D	++++		C5-15	6.0	0	—	D	0
	C5-47	6.4	0	—	K	0		C5-23	12.0	2	90	D	++
	C5-45	9.7	0	—	K	0		C5-29	13.0	0	—	D	0
	C5-32	10.0	0	—	D	0		C5-27	14.9	0	—	K	0
	C5-14	11.5	3	129	D	+++		C5-33	14.9	0	—	K	0
	C4S-30	14.9	2	36	K	0							
	C5-22	14.9	0	0	K	0							
F	F6-3	4.5	0	—	K	0	F	F5-15	15.0	0	—	K	0
	F5-14	10.0	5	76	D	0		F6-2	15.0	0	—	K	0
	F5-2	15.0	3	126	K	0*							

* Atypical pulmonary tissue inoculated into guinea pigs which failed to develop tuberculosis.

killed and carefully autopsied. Guinea pig inoculation was resorted to in the case of the least doubt.

Results of Experiment of 1941–42

It will be seen in Table III that there were two cases of fatal tuberculosis in the unirradiated half of the manifold and one case in the irradiated section. All three rabbits were members of the family C, of low resistance to tuber-

culosis. None of the rabbits of the highly resistant A family developed active tuberculosis nor did the small number of F rabbits, of low resistance to the disease, acquire demonstrable tuberculosis. It will be further seen that seven additional rabbits in the unirradiated half of the cage developed positive tuberculin reactions which were observed on two to twelve separate occasions. However, none of these animals showed macroscopic tuberculous changes in any organs at death; nor did their lungs harbor virulent tubercle bacilli, as demonstrated by guinea pig inoculation in four of the rabbits. On the other hand, only two rabbits in the irradiated half of the cage showed positive reactions to tuberculin on one or two occasions. The maximum volume of these tuberculin reactions is given in the table.

The significance of these findings will be discussed later more fully. At this point it may be stated, assuming the specificity of the tuberculin reaction, that there were 9 control rabbits that showed evidence of intimate interaction between the tubercle bacillus and the host. In the irradiated section of the manifold, on the other hand, there were only three such cases, though the contacts were exposed to the same sources of contagion for approximately the same length of time and had the same genetic constitution as the contacts in the unirradiated section. It would seem, therefore, that the ultraviolet radiation exerted a definite, though incomplete, protective influence on the contagion of tuberculosis.

The total incidence of fatal tuberculosis in the unirradiated half of the manifold was very low in this experiment, 11.1 per cent, as contrasted with an incidence of 76.5 per cent in a similar contagion experiment performed in this manifold with the same rabbit families in 1939–40.

Seeking an explanation for this discrepancy, it became apparent that there were two differences in the setup of these two experiments: (1) peat moss was used as bedding for the sources of contagion in 1939–40, while in the present experiment, conducted in 1941–42, peanut shells were used; (2) no ultraviolet radiation was present in the room in the former experiment, whereas in this study, in one portion of the room there was ultraviolet radiation. Recalling the old observation (2) that tuberculous contagion is uniformly distributed throughout the air of an enclosure which houses animals shedding tubercle bacilli, an explanation for the above noted discrepancy between the two experiments became obvious, *i.e.*, the ultraviolet lamps present in the experimental half of the room had reduced the total concentration of bacteria in the room so that the intensity of contagion was much less than in the 1939–40 experiment. To test this concept, an entirely new setup was instituted.

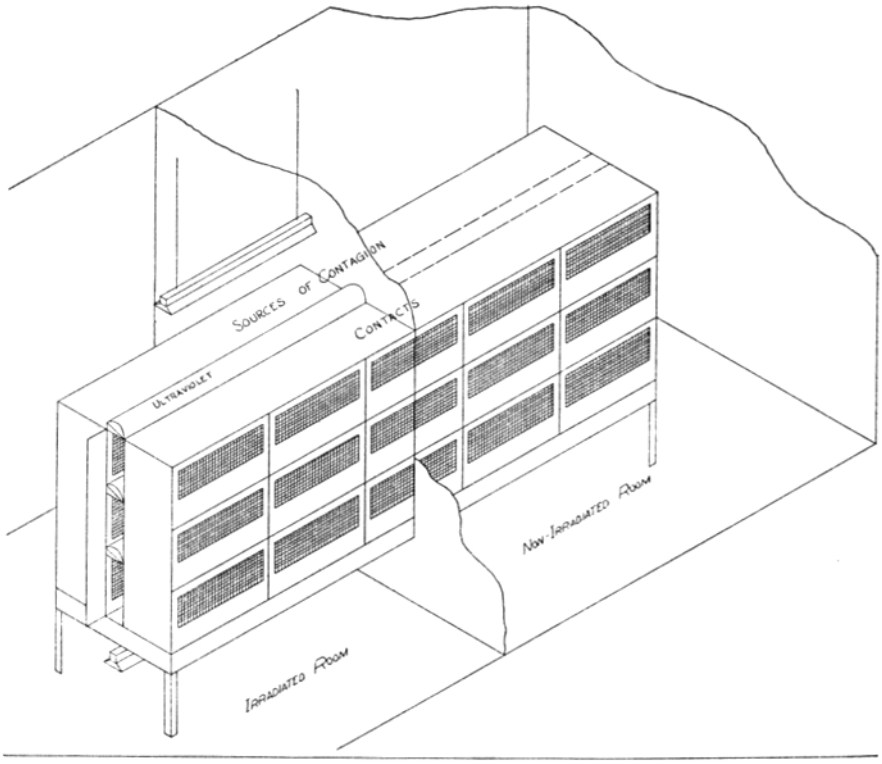
Materials and Methods

Experiment of 1942–43

The room in which the experiment was to be conducted was completely divided from floor to ceiling by a solid wooden partition so placed that it divided the manifold in

half. One section of the manifold was in one room, while the other section was in the adjoining room. There was no direct continuity of the air in the two rooms. One of these rooms was irradiated. The other was not irradiated. As in the previous experiment, the interior of the two sections of the manifold were completely separated from each other by an air-tight metal partition.

In the experimental room an ultraviolet lamp emitting monochromatic rays of 2537Å was suspended horizontally from the ceiling. It was situated above the



TEXT-FIG. 2. Experiment of 1942–43.

center of the manifold, along its long axis and reflected downwards by a parabolic reflector. Another lamp was fixed horizontally to the bottom of the manifold along the center of its long axis and reflected toward the floor. In the space between the sources of contagion and the contacts, ultraviolet lamps, extending horizontally over the entire length of this section of the manifold, were placed above the ceiling of each of the three tiers. In these ceilings slits had been previously cut to permit the uniform irradiation of the air spaces below them. The reflectors carrying the lamps above each tier were tilted at an angle of 45° in such a way that, while the air between the sources of contagion and the contacts was effectively irradiated, the contacts themselves were exposed to little direct ultraviolet radiation (Text-fig. 2). This method of

irradiation differed radically from that of the previous experiment in the following respects: (*a*) Experimental and control animals were in two separate rooms. Radiation was present in the experimental room, whereas, in the control room no radiation was present. In the previous setup the experimental portion of the room was irradiated but the air in the two halves of the room formed a single continuum. (*b*) The irradiation of the space between the sources of contagion and the contacts in this experiment was of the same intensity throughout the length of the section in each tier, an average of 230 μw. and a minimum of 150 μw. per cm.^{2} (Table IV). In the previous experiment this barrier had diminished in intensity from one end of the section to the other with an average intensity of only 40 μw. per cm.^{2} and a minimum of only 12 μw.

TABLE IV

The Intensity of Ultraviolet Energy in the Space between the Infected and Exposed Rabbits Relative to the Position of the Contact Cages in the Manifold of the Irradiated Room

Experiment of 1942–43

	Ultraviolet lamp			Ultraviolet lamp		Average radiant energy in tier space
Cage No.	1	2	3	4	5	
Radiant energy, μw.	156	195	156	253		203
	Ultraviolet lamp			Ultraviolet lamp		
Cage No.	6	7	8	9	10	
Radiant energy, μw.	273	273	234	234	195	242
	Ultraviolet lamp			Ultraviolet lamp		
Cage No.	11	12	13	14	15	
Radiant energy, μw.	273	351	234	234	195	257

In order to increase the intensity of the exposure the rabbits which were to serve as sources of contagion were all infected with 0.000,1 to 0.001 mg. of highly virulent bovine type tubercle bacilli directly into the substance of the kidney. This brought about a continuous elimination of culturally demonstrable tubercle bacilli in the urine of all rabbits which began the 3rd week after infection.[2] Before the rabbits which were to serve as contacts were placed into these rooms it was ascertained by culture that all the sources of contagion were shedding tubercle bacilli. As in the previous experiment, four rabbits were placed in each run, in each tier and, in case of death, were replaced by similarly infected rabbits. Peat moss was used for bedding the sources of contagion instead of the peanut shells of the experiment of 1941–42.

[2] Acknowledgment is hereby made to Sylvia Brener for the determination of the number of bacilli shed in the urine of these rabbits following different periods of inoculation.

As in the last experiment the sources of contagion in each of the three runs of the experimental and control room were interchanged daily to maintain a uniform intensity of contagion for the contacts of both rooms.

The contacts in the experimental and control rooms were litter mates of the same highly inbred, genetically uniform rabbits of the highly resistant A family and the families C and F, of low resistance. The disposition of the rabbits in both rooms is given in Table V. It will be seen that the genetic homogeneity of the experimental

TABLE V

The Distribution of the Contacts in the Cages of the Manifold, Their Sex, Age in Months, and Their Parents

Experiment of 1942–43

Unirradiated room					Irradiated room				
1	2	3	4	5	1	2	3	4	5
A8=19 ♂, 10.5 A7=15 × A7=1	C5-50 ♂, 16.5 C4S-27 × C4S-28	A8=29 ♂, 8.0 A7=13 × A7=1	C6-26 ♂, 4.5 C5-46 × C5-40	A7=36 ♂, 12 A6=22 × A6=9	A8=39 ♀, 7.5 A7=15 × A7=1	C5-44 ♀, 19.5 C4S-27 × C4S-28	A8=23 ♂, 10.3 A7=13 × A7=1	C6-30 ♂, 4.5 C5-46 × C5-40	A7=37 ♂, 11.9 A6=22 × A6=27
6	7	8	9	10	6	7	8	9	10
C6-1 ♂, 9.0 C5-46 × C5-40	A7=44 ♂, 6.8 A6=22 × A6=27	C6-9 ♂, 8.4 C5-39 × C5-40	A8=51 ♀, 5.5 A7=3 × A6=27	C6-32 ♀, 4.0 C5-39 × C5-40	C6-2 ♂, 9.0 C5-46 × C5-40	A7=40 ♂, 8.9 A6=22 × A6=27	C6-13 ♂, 8.4 C5-39 × C5-40	A8=49 ♂, 5.6 A7=3 × A6=27	C6-31 ♂, 4.0 C5-39 × C5-40
11	12	13	14	15	11	12	13	14	15
A7=26 ♀, 14.0 A6=22 × A6=18	F6-25 ♂, 8.0 F5-18 × F5-1	A8=43 ♂, 6.0 A7=13 × A7=25	F6-14 ♂, 11.0 F5-18 × F5-1	A7=31 ♂, 12.0 A5=26 × A6=9	A7=28 ♂, 14 A6=22 × A6=18	F6-21 ♂, 8.0 F5-18 × F5-1	A8=52 ♂, 5.0 A7=15 × A7=1	F6-15 ♂, 11 F5-18 × F5-1	F5-27 ♂, 17.1 F4-63 × F4-48

1 = cage 1; A8=19 = contact of the eighth inbred generation of the A family; sex; 10.5 is the age of the contact in months at the beginning of exposure. A7=15 × A7=1 are the parents of A8=19.

and control animals was very high indeed. Since the irradiated barrier between the sources of contagion and the contacts in all the three tiers of the experimental section of the cage was uniform throughout its length the contacts, both experimental and control, were not rotated as in the previous experiment but left in the same position throughout the duration of the investigation.

Results of Experiments of 1942–43

As can be seen from Table VI the results of this experiment are clear and decisive. Out of the 15 contacts exposed in the unirradiated room 11, or 73 per

cent, developed tuberculosis which was fatal in nine cases during the course of the experiment. The remaining two rabbits were killed at the termination of the investigation and were found to have moderate tuberculosis from which, undoubtedly, they would have died in the course of several months. In addition, three more rabbits developed positive tuberculin reactions which were

TABLE VI

The Effect of Ultraviolet Irradiation on Natural Air-borne Contagion of Tuberculosis in Contacts of Rabbit Family A, of High Inherited Natural Resistance, and in Families C and F, of Low Inherited Natural Resistance to the Disease

Experiment of 1942–43

Rabbits exposed in unirradiated room							Rabbits exposed in irradiated room						
Family	Rabbit No.	Duration of exposure	No. of times tuberculin positive	Maximum tuberculin reaction in mm.[a] of inflammation	Killed (K) or died (D)	Extent of tuberculosis at death	Family	Rabbit No.	Duration of exposure	No. of times tuberculin positive	Maximum tuberculin reaction in mm.[a] of inflammation	Killed (K) or died (D)	Extent of tuberculosis at death
		mos.							*mos.*				
A	A8=19	5.6	7	368	D	++++	A	A8=23	6.5	0	—	D	0
	A8=51	6.3	7	741	D	+++		A8=39	8.9	0	—	D	0
	A7=26	7.3	7	372	D	++++		A7=37	11.6	0	—	K	0
	A8=43	9.7	4	475	D	0		A7=40	11.6	0	—	K	?*
	A7=31	10.8	15	1350	D	0		A8=49	11.7	0	—	K	0
	A8=29	11.6	7	150	K	++		A7=28	11.7	0	—	K	0
	A7=36	11.6	11	260	K	++		A8=52	11.8	0	—	K	0
	A7=44	11.6	0	—	K	0							
C	C6-9	5.2	7	1330	D	++++	C	C6-30	5.7	0	—	D	0
	C6-32	5.7	7	432	D	++++		C5-44	11.6	0	—	K	0
	C5-50	6.1	7	672	D	++++		C6-2	11.7	0	—	K	0
	C6-26	9.2	2	213	D	+±		C6-13	11.7	0	—	K	0
	C6-1	11.6	3	153	K	0		C6-31	11.7	0	—	K	0
F	F6-25	8.8	4	342	D	++++	F	F5-27	11.7	0	—	K	0
	F6-14	10.4	3	141	D	++++		F6-21	11.8	0	—	K	0
								F6-15	11.8	0	—	K	0

* Guinea pig inoculation of a questionable pulmonary lesion demonstrated living, virulent tubercle bacilli.

demonstrated 3 to 15 times as detailed in Table VI. Only a single rabbit escaped all evidence of interaction with the tubercle bacillus in these control contacts. Under this intensity of contagion rabbits of both high and low resistance to the disease developed fatal tuberculosis.

On the other hand, not a single rabbit of the 15 experimental contacts of the same genetic constitution, exposed to the same sources of contagion and for an even longer average period, showed any tuberculous changes on scrupulous examination at autopsy. One rabbit, A7=40, killed after 11.6 months of

exposure showed a questionable minute focus. Neither in the direct smear nor in the fixed section could tubercle bacilli be seen after prolonged search. This focus was composed of epithelioid and giant cells without caseation and was broken up by strands of young fibroblasts. However, upon guinea pig inoculation, this minute regressive tubercle produced tuberculosis in a lymph node draining the site of injection. There was not a single case of a positive tuberculin reaction in any of the 15 contacts in the irradiated room including A7=40.

DISCUSSION

The experiments detailed above demonstrate the protective influence of ultraviolet irradiation of the air against natural air-borne contagion of tuberculosis in rabbits. When the intensity of irradiation was low, it reduced the incidence of tuberculosis to a marked degree and completely protected rabbits of high natural resistance to tuberculosis from acquiring demonstrable disease. However, a small proportion of rabbits of low natural resistance developed fatal tuberculosis. When the intensity of irradiation was high it completely protected all rabbits, whether of high or low resistance, from an intensity of contagion which caused progressive tuberculosis within a period of one year in 73 per cent of the control rabbits of the same genetic constitution, exposed to the same sources of contagion for the same time. If it is borne in mind that this contagion was very much greater than can ever occur in human life, it is clear that ultraviolet irradiation may be effective in the control of human tuberculosis, for the highest annual attack rate among negro infants, the most susceptible of our population, does not exceed 5 per cent (5).

The 1941–42 experiment demonstrates several important points. A comparison of this experiment with that of 1939–40, as given in Table VII, shows that the incidence of fatal tuberculosis in the unirradiated half of the room was 7 times less in the first mentioned experiment, which was conducted on rabbits of the same genetic constitution, exposed to approximately the same number of tubercle bacilli-shedding sources of contagion for even a longer period of time. There were two differences between these two experiments. In the older experiment, peat moss bedded the sources of contagion and no ultraviolet radiation was present in the room. In the 1941–42 experiment, the bedding was peanut shells and ultraviolet radiation was present. It is not unlikely that peanut shells reduced the intensity of contagion for peat moss absorbs the urine well and peanut shells, poorly. Since the main source of contagion in these experiments is the urine of the rabbits, it is probable that fewer tubercle bacilli-bearing particles were thrown into the air by the movement of the rabbits bedded with peanut shells than of those bedded with peat moss. What is certain from the 1942–43 experiment, however, is that ultraviolet energy, in sufficient concentration, can eliminate air-borne tuberculous contagion almost completely. Since it was demonstrated in an old experiment (2) that con-

tagious material given off by tuberculous animals in one part of an enclosure is uniformly distributed throughout the air of that space, it is clear that, conversely, if one part of a room is subjected to a bactericidal agent, the total bacterial concentration will be reduced throughout the continuum. Therefore, there resulted a sevenfold reduction in the incidence of fatal tuberculosis in the 1941–42 experiment as compared to the 1939–40 experiment. The efficacy of ultraviolet irradiation is therefore plain.

It is assumed in this study that the tuberculin reaction in rabbits is specific. It indicates the penetration into and interaction with the tissues of tubercle bacilli in sufficient concentration to produce the specific allergic response. The work of Opie and Freund (6) supports this assumption. The complete absence of any positive tuberculin reactors, as well as of any other gross evidence of

TABLE VII

Relation between the Incidence of Fatal Tuberculosis in the Experiments of 1939–40 and 1941–42 and the Presence of Ultraviolet Energy in the Exposure Room

Date of experiment	No. of rabbits exposed	Average duration of exposure	Sources of contagion with tubercle bacilli in smears of urine	Bedding of sources of contagion	Presence of ultraviolet radiation in room	Incidence of fatal tuberculosis
		mos.	*per cent*			*per cent*
1939–40	17	9.2	34.6	Peat moss	Absent	76.5
1941–42	18	11.7	32.3	Peanut shells	Present	11.1

tuberculosis, among the contacts in the irradiated room of the 1942–43 experiment speaks strongly for the above interpretation.

If we take into consideration the positive reactors to tuberculin in the 1941–42 experiment which showed no lesions at death, the contacts living in the irradiated section of the cage were protected better than those in the control section, obviously, because of the greater intensity of the rays in this portion of the room. That one rabbit in the irradiated section of the cage contracted tuberculosis and that two additional animals developed tuberculin reactions is due to the fact that for 6 days in each month these rabbits were separated from the sources of contagion by a barrier of ultraviolet rays lower than 20 μw. per cm.^{2}. This intensity of irradiation is insufficient to kill all tubercle bacilli for it has been shown that even 3 seconds' exposure to 120 μw. cm.^{2} of 2537 Å killed only 94 per cent of the tubercle bacilli suspended in the air (3). That the degree of suppression of the contagion of tuberculosis is a function of the intensity of the radiant energy is demonstrated in the 1942–43 experiment where the barrier of ultraviolet radiation between the contacts and the sources of contagion had an average intensity of 230 μw. per cm.^{2}. Here none of the

fifteen rabbits, not even those of low natural resistance, showed any gross evidence of tuberculosis, even a positive tuberculin reaction, while eleven of the fifteen genetically homogeneous controls, both of low and high resistance, exposed to the same sources of contagion for the same time, developed fatal tuberculosis and three additional rabbits developed positive tuberculin reactions without demonstrable lesions at death. Only one of these fifteen rabbits failed to show any evidence of tuberculosis.

The almost all or none character of the 1942–43 experiment is most likely due to the completeness of exclusion of all variables in the control and experimental animals except that of the presence or absence of ultraviolet radiation. Infection is due to the interplay of the causative organism and host resistance. In this experiment both factors were identical in the two rooms. The genetic constitution, which determines the mode of response of the tissues to the tubercle bacillus was identical in both. The tubercle bacillus, both in quantity and quality, was also made to be the same by the maneuver of interchanging the sources of contagion daily between the control and experimental rooms. Since the variable studied was a physical factor it is not astonishing that the results of this biological experiment were mathematically exact.

The question arises: How did the ultraviolet energy suppress the tuberculosis in the contacts of the irradiated room? It is conceivable that the rays might have exercised some obscure influence on the physiological responses of these contacts to the tubercle bacillus, since it is recognized clinically that ultraviolet radiation has a beneficial influence on some forms of tuberculosis. If this were the case, one might expect less rapidly progressive tuberculosis in the experimental room. The almost complete suppression thereof in the 1942–43 experiment speaks strongly for the bactericidal properties of the rays as the effective agent in this protection. This experiment also gives convincing evidence that the contagion of tuberculosis in these studies are primarily air-borne, for were the contagion carried by other means no such complete elimination of its effects could be expected. This result also suggests that the tubercle bacilli-laden particles concerned in the natural contagion of tuberculosis in rabbits must be of very small size, such that the rays could effectively sterilize.

It is noteworthy that except for an occasional conjunctivitis no evidence of any deleterious effects of the ultraviolet radiation was found in the exposed rabbits.

CONCLUSIONS

1. Ultraviolet irradiation of the air of a room exercises a protective influence against natural air-borne contagion of tuberculosis in rabbits.

2. When the radiant energy is of low intensity it reduces considerably the incidence of tuberculosis.

(*a*) It completely protects rabbits of high natural resistance from acquiring demonstrable disease though they become tuberculin sensitive.

(*b*) It fails to protect a small proportion of rabbits of low natural resistance from fatal tuberculosis.

3. When the radiant energy is of high intensity all rabbits, whether of high or of low natural resistance, are almost completely protected from a contagion so severe that it is fatal to the great majority of rabbits of the same genetic constitution not protected by these rays. The protected rabbits do not develop tuberculin sensitivity.

4. The contagion of tuberculosis in these studies is air-borne and the radiant energy exercises its protective influence by its bactericidal properties. It is probable that ultraviolet irradiation may control air-borne contagion of human tuberculosis.

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