

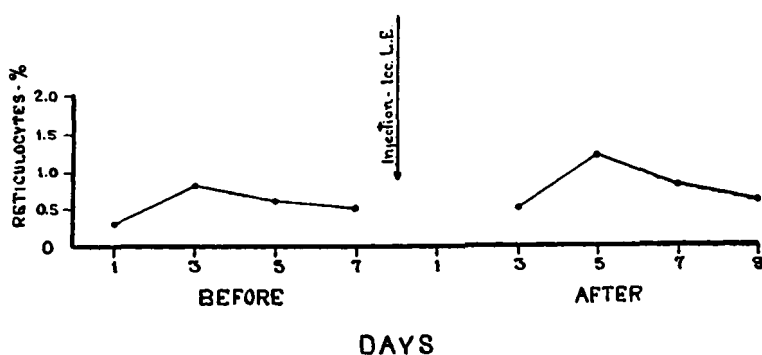


FIG. 2.

Mean reticulocyte percentage obtained in 10 pigs (Group II) before and after injection of liver extract.

Results. The average of reticulocyte counts for all animals obtained on the days following intramuscular injections is given in Figs. 1 and 2.

None of the animals in Group I gave a reticulocyte response of over 2%. A reticulocyte count of 4% was obtained in one of the animals of Group II on the fifth day after injection. This was the only guinea pig of both groups in which the reticulocyte response was significantly greater than 2%, which is considered as the index of reactivity by Jacobson. Two other animals of Group II gave reticulocyte counts of 2.1%, which might be considered as reactive. This rise occurred on the fifth day following injection. In other words, only 3 of the 20 animals used in the experiment were found "reactive" to the method of Jacobson.

The results obtained lead us to consider the method as not sufficiently sensitive in the evaluation of the antianemic principle.

10138 P

Rôle of Inherited Natural Resistance to Tuberculosis.

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The pioneer studies of Lewis and Wright¹ on inheritance factors in tuberculosis in guinea pigs as well as the writer's observations² have prompted a continuance of their studies.

¹ Wright, S., and Lewis, P. A., *Am. Naturalist*, 1921, **55**, 20.

² Lurie, M. B., *J. Exp. Med.*, 1933, **58**, 305.

By brother and sister inbreeding of rabbit groups for 4 to 5 generations families have been developed which exhibit varying, inherited, specific resistance to tuberculosis. This has been determined by exposing the succeeding generations of the different families to artificially infected rabbits in specially constructed large cages separated in the middle by a fine wire mesh screen. On one side of the screen are placed rabbits artificially infected with virulent bovine tubercle bacilli. The bacilli shed by these rabbits, chiefly in their urine, are inhaled by representatives of the different rabbit families which are placed simultaneously on the opposite side of the screen. At stated intervals the contacts are tested with tuberculin. Since by this method the disease acquired by the contacts is nearly always of pulmonary origin, their lungs are X-rayed at the same time. The onset and progress of the disease are thus determined.

It was found, after excluding all known environmental factors that the genetic constitution of the rabbit *per se* may determine the type of disease developed on first natural contact with the tubercle bacillus. Those hereditarily most susceptible develop a disease of



FIG. 1.

Rabbit H2-2 of the H family. Primary focus in upper lobe of right lung; massive caseation of right tracheo-bronchial nodes; miliary tuberculosis of lungs; tuberculosis of ribs, kidney and bone marrow. Duration of disease—3 months.

short duration analogous to infantile tuberculosis. A primary focus develops in the lung, which is accompanied by massive caseation of the draining tracheobronchial lymph nodes. Soon this primary focus undergoes softening and the released bacilli invade the blood stream, so that the animal dies shortly of generalized miliary tuberculosis (Fig. 1). The animals of somewhat greater resistance develop a disease of longer duration analogous to the so-called childhood type with caseous pneumonia, massive involvement of the tracheo-bronchial nodes and large destructive nodular lesions of hematogenous origin in different parts of the body such as the kidneys, eyes, bones, etc. (Fig. 2). The most resistant family, on



FIG. 2.

Rabbit F2-3 of the F family. Massive caseous pneumonia of both lungs with extensive caseation of left tracheo-bronchial lymph node; extensive tuberculosis of both kidneys; tuberculosis of pleura; destructive tuberculosis of one eye; tuberculosis of trachea and bone marrow. Duration of disease—5 months.

first exposure to the tubercle bacillus, without previous vaccination, develops a disease of much greater chronicity which is characterized by a localized ulcerative pulmonary phthisis in which the draining tracheo-bronchial lymph nodes and the remaining organs are almost always spared. Anatomically this disease has the distinguishing features characteristic of adult type pulmonary tuberculosis in man

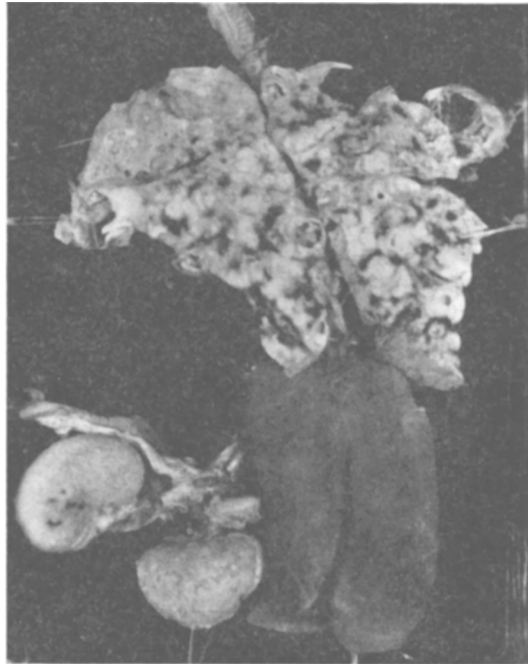


FIG. 3.

Rabbit A2-10 of the A family. Localized ulcerative pulmonary phthisis; draining tracheo-bronchial node tied with string to trachea of small size and grossly normal; healed, small, scarred tubercles in kidneys. Duration of disease—7 months.

(Fig. 3). Hitherto adult pulmonary phthisis has been considered as resulting solely from a reinfection.

Table I summarizes the incidence of caseous tuberculosis of the lymph nodes draining the portal of entry in rabbit families exposed to respiratory contagion. The families are arranged in the order of decreasing resistance. It will be noted that 9 out of 10 rabbits of the most resistant A family have escaped involvement of the hilum lymph nodes entirely, while all of the rabbits of the most susceptible families developed extensive tuberculosis of the draining tracheo-bronchial lymph nodes. It is noteworthy that a considerable proportion of the rabbits of the B family, of intermediate resistance, developed slight hilum lesions. While the number of observations is small, the difference between the A family and all the others is so great that it suggests an all or none reaction and therefore appears to have considerable significance.

While contagion experiments simulate the mode of infection in man, the dosage of bacilli to which the contacts of the different families are exposed is unknown and inconstant, therefore the resistance

TABLE I.
Incidence of Tuberculous Involvement of Lymph Nodes Draining the Portal of Entry in Rabbit Families Exposed to Natural Respiratory Contagion.

Family	Generation	No. of rabbits	Rabbits with extensive tuberculous of draining lymph nodes		Rabbits with slight tuberculous of draining lymph nodes		Rabbits with no gross tuberculous of draining lymph nodes	
			No.	%	No.	%	No.	%
A	2nd and 3rd	10	0	0	1	10	9	90
B	2nd, 3rd and 4th	7	4	57	3	43	0	0
G	2nd	6	4	67	0	0	2	33
D	2nd and 3rd	5	4	80	0	0	1	20
H	2nd and 3rd	7	6	86	0	0	1	14
F	2nd and 3rd	7	7	100	0	0	0	0
C	2nd and 3rd	7	7	100	0	0	0	0

TABLE II.
Resistance of Rabbit Families to Inoculation of Standard Doses of Bovine Tubercle Bacilli.

.2 mg Ravenel intracultaneously		.001 mg Ravenel per kilo intravenously	
Rabbit No. generation and family	Survival in days	Rabbit No. generation and family	Survival in days
A 3-9	291		
A 3-11	296		
A 3-12	241*		
Avg	276 $\pm$ 25		
B 3-5	176	B 3-12	125*
B 3-6	123*	B 3-13	196
B 3-7	196	B 3-16	170
		B 3-15	159
Avg	165 $\pm$ 30	Avg	162 $\pm$ 25
H 2-19	123	H 2-29	79
H 2-22	108	H 2-31	73
H 2-23	133	H 2-26	78
H 2-24	134	H 2-32	82
Avg	124 $\pm$ 21	Avg	78 $\pm$ 4

*Tuberculosis complicated by an intercurrent infection.

of these families to tuberculosis has been tested by the inoculation of standard quantities of tubercle bacilli by various routes. Two such titrations of the families A, B, and H are presented in Table II.

It is clear from this table that the A family is most resistant. The B family is of intermediate resistance and the H family of lowest resistance of the 3 families considered. This is the same order of resistance that these families exhibited when they acquired tuberculosis by contagion.

In the succeeding paper further corroborative evidence is presented of the relative resistance of these families to standard doses of tubercle bacilli.

10139 P

Nature of Inherited Natural Resistance to Tuberculosis.

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In an endeavor to elucidate the physiological bases of the inherited constitutional resistance to tuberculosis in the families discussed in the preceding report the following experiment was performed. About 4 litter mates of each of the third or fourth gen-