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Immunity Phenomena in Transmissible Leucosis of Fowls.*

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The discoverer of transmissible leucosis, Ellermann, thought that there is no immunity to leucosis because fowls resisting one inoculation may succumb to reinoculation. More recent knowledge gained on immunity against Rous tumors (Rous, Mottram, Andrewes, Mueller, etc.) necessitates a revision of this conclusion.

Active immunity. Cell-free virus and leucemic cells must be considered separately, because leucemic cells behave like neoplastic cells and specific immunity is not known to develop in tumor-bearing animals. Furthermore the virus itself may be protected from immune bodies by association with cells. Accordingly 8 possibilities were tested with the following results:

TABLE I.

Material first injected	Result	Material reinjected	No. fowls injected	No. transmissible leucosis	No. lymphoid leucosis
Cell-free	Negative	Cell-free	16	6	1
" "	Leucosis, recovery	" "	4	0	0
" "	Negative	Cell-containing	8	4	1
" "	Leucosis, recovery	"	7	3	0
Cell-containing	Negative	Cell-free	3	0	0
" "	Leucosis, recovery	" "	4	0	1
" "	Negative	Cell-containing	4	0	1
" "	Leucosis, recovery	" "	10	1†	0

† Succumbed to leucosis after 6 reinjections with whole leucemic blood.

The fowls resistant both to cell-free virus and leucemic cells are those that were previously injected with material containing live leucemic cells. Their resistance may in part be due to antibodies against the free virus; antibodies active against leucemic cells have however thus far not been demonstrated. Resistance to reinjection with cells if not caused by acquired immunity, may be either an inherited character becoming manifest through elimination of susceptible fowls by the first injection, or a non-specific resistance-increase due to the first injection, or to other conditions, such as advancing age.

The reinjections were made with 0.5 to 1 cc. of leucemic blood

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or plasma, estimated to contain 10,000 to 1,000,000 infective doses. It is possible that smaller amounts may reveal some immunity in groups 1, 3, 4. Among the 56 fowls tested, 4 had lymphoid leucosis (as compared to 14 with transmissible leucosis). They were grouped as negative, because according to previous investigations lymphoid leucosis is not caused by the agent of transmissible leucosis.

Passive immunity. When leucemic plasma of fowls was mixed with the serum of presumably immune fowls and injected within about 20 minutes, a mild but distinct protection was observed. Of the 27 fowls thus inoculated 26% developed leucosis as compared with 40% of the 15 fowls given a similar mixture containing normal instead of immune serum. Protection was complete against at least 1000 M.L.D. when mixtures of virus and immune serum were incubated at 37.5°C. for one hour, as shown in the following experiment.

Of 4 fowls given 2.5 cc. of a mixture of 3 cc. normal serum plus 0.5 cc. leucemic plasma, 3 developed leucosis after 21 days. Of 4 fowls receiving 2.5 cc. of the same normal serum plus 0.0005 cc. of leucemic plasma 3 developed leucosis, but after 40 days. All of 8 fowls receiving similar mixtures containing immune instead of normal serum remained free from leucosis. The immune serum was obtained from fowls resisting several inoculations of whole leucemic blood.

Protection against material containing leucemic cells on the contrary thus far has not been demonstrated. In 5 experiments involving 23 fowls inoculated with a mixture of immune serum plus leucemic cells, 61% of the former group developed leucosis, and 53% of the latter.

Failure to produce virus-free leucosis in the fowl. The experiments described indicate that fowls develop antibodies against the cell-free virus. The possibility suggests itself that virus-free leucosis might be produced by introducing leucemic cells, which are apparently neoplastic, into fowls immune to the virus.

With this in view a fowl found resistant to the free virus was injected with leucemic cells. As soon as its blood indicated incipient leucosis plasma and cells were injected each into 3 chickens. One of each group developed leucosis. Two months later, when the disease was advanced, this test was repeated in 8 fowls, half of which were injected with plasma, half with cells; all developed leucosis.

This experiment suggests that the filterable agent when in association with cells is protected against antibodies and that during

cell-division it is handed over to the daughter cells unharmed by viricidal bodies. A repetition of the last experiment awaits fowls highly immune to the virus, but susceptible to leucemic cells.

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Readily Acid-Hydrolysable Phosphorus of the Blood in Infants with Rickets.

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The P fraction in red blood cells, readily hydrolysable by N mineral acid, was estimated in non-rachitic and rachitic infants.

The method of Lohmann[1] for this fraction in muscle, as adapted by Barrenscheen and Vasarhelyi[2] for blood, was used with slight modification. One volume of blood was added to 4 volumes of 10% trichloracetic acid and the mixture filtered. Ortho-phosphate was determined by the method of Fiske and Subbarow.[3] Two cc. of 2 N HCl were added to two cc. of the filtrate, the mixture was heated at 100°C. for 10 minutes and the P again determined. From the amount of P freed in this way, the amount of ortho-phosphate and the hematocrit reading, the whole blood and red cell content of this fraction was calculated.

Variations in time of heating from 10 to 15 minutes gave no significant difference in the amount of P freed. No difference was noted between the use of H_2SO_4 and HCl as the hydrolyzing acids. This fraction is gradually split in the trichloracetic acid filtrate, from 0.5 to 1.0 mg. being freed in the first 24 hours at ice-box temperature. It does not give the color reaction for pyro-phosphate described by Davenport and Sacks.[4]

The results in non-rachitic and rachitic children are shown in Tables I and II. The values have been calculated for whole blood and for the red cells. Values for the ortho-phosphate content of serum, whole blood and red cells are included in the tables.

The average value for this fraction in the whole blood of non-rachitic children was 5.20 mg. % as P, with a standard deviation of 0.86 mg. % and a coefficient of variation of 16.5%. The average

[1] Lohmann, K., *Biochem. Z.*, 1928, **202**, 466.

[2] Barrenscheen, H. K., and Vasarhelyi, B., *Biochem. Z.*, 1931, **230**, 330.

[3] Fiske, C. H., and Subbarow, Y., *J. Biol. Chem.*, 1925, **66**, 375.

[4] Davenport, H. A., and Sacks, J., *J. Biol. Chem.*, 1928, **81**, 469.