which were inactive by animal inoculation. Moreover, multiplication of minute quantities of virus in tissue cultures was not inhibited by the presence in them of formolized vaccines in which the formalin was neutralized by ammonia. It was thus possible to determine that an amount of vaccine (1 cc.)—the immunizing dose—contained no detectable active virus.

8469 P

Host Age and Cell Metabolism in Mouse Lymphatic Leukemia.

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During the course of experiments on the relationship of cell virulence to cell metabolism, certain results indicated that the age of the host influenced the metabolism of transmitted leukemia cells. To investigate the effect of age, the following experiments were performed: Mice of 2 age groups (6-8 weeks and 6-8 months) were inoculated with the same transfer cells of a transmission line M-liver. Metabolic measurements, namely Q_{O_2}, $Q_{CO_2}^{O_2}$ and $Q_{CO_2}^{N_2}$ in Ringer's solution[6] were made on the lymph nodes 4 days after inoculation. The mice were of strain C 58, 100% of which develop lymphatic leukemia after inoculation with line M-liver; 90% develop spontaneous lymphatic leukemia after 6 months of age.[1] So far as could be determined, *i. e.,* from palpation and blood counts before inoculation and autopsy, no evidence of spontaneous leukemia was found in mice used. A summary of the metabolic results is presented in Table I. The metabolism was significantly decreased in every characteristic studied. The decrease in Q_{O_2} of the leukemic lymph nodes parallels the decrease found in normal lymphoid tissue previously reported.[2] On the other hand the decrease in $Q_{CO_2}^{O_2}$ and $Q_{CO_2}^{N_2}$ is actually greater than the table indicates, for it has been found that the normal glycolytic rates are higher in 6-8-month-old mice than in 6-8-weeks-old mice. In other words the actual excess glycolysis, both aerobic and anaerobic produced by the leukemia cells is less than the values in the table.

6 Warburg, O., *Metabolism of Tumours,* London, Constable & Co., Ltd., 1930.

1 MacDowell, E. C., and Richter, M. N., *Arch. Path.,* 1935, **20**, 709.

2 Victor, J., and Potter, J. S., *Brit. J. Exp. Path.,* 1935, **16**, 243.

TABLE I.
Metabolic Effects of Age of Host on Cells of Line M Liver.
Young 6-8 weeks, Old 6-8 months.

	No. of Observation	Q_{O_2} Mean	S.D.	$Q^{O_2}_{CO_2}$ Mean	S.D.	$Q^{N_2}_{CO_2}$ Mean	S.D.
(1) Young	9	5.26±.12	.55	8.44±.25	1.11	18.36±.44	1.96
(2) Old	11	4.63±.10	.50	6.86±.22	1.09	16.39±.37	1.84
Difference (1) — (2)		*.63*±.15		*1.58*±.33		*1.97*±.58	
Diff. / P.E. Diff.		4.2		4.8		3.4	

To test the reversibility of the age effect, the following experiments were performed. The metabolism of the lymphoid cells of a mouse of Strain C 58 with spontaneous lymphatic leukemia was determined. In addition to the other characteristics the R.Q. was measured in the presence of 0.2% glucose.[3] The cells of the spleen were inoculated into old (6-8 months) and young (6-8 weeks) mice of this Strain C 58; then splenic transmissions were performed in 2 series through old mice with young controls and through young with old controls. Schematically this is represented as follows:

Spontaneous Case.

Control	Control
Old	Young
Young—Old	Young—Old
Young—Old	Young—Old
Etc.	Etc.

This line was called line 0.

It seemed that in addition to age effects the experiment might throw some light on metabolism associated with changes in virulence. It has been found that the virulence of a transmission line of leukemia increases very rapidly in the early transfers. Thirteen transfers were studied. About 380 observations were made. The results are summarized in Table II. Table III shows a comparison of the

TABLE II.
Metabolic Rates of Lymph Nodes of Mice Inoculated with Line O.
Old 6-8 months, Young 6-8 weeks.

Group	Q_{O_2} Mean	S.D.	R.Q. Mean	S.D.	$Q^{O_2}_{CO_2}$ Mean	S.D.	$Q^{N_2}_{CO_2}$ Mean	S.D.
(1) Old-Old	4.65±.06	.48	.773±.003	.022	2.18±.06	.47	8.06±.25	1.98
(2) Old-Young	4.95±.08	.51	.840±.005	.027	2.65±.05	.33	9.33±.31	2.19
(3) Young-Young	5.31±.11	.75	.898±.003	.021	2.64±.16	1.05	9.70±.24	1.58
(4) Young-Old	4.81±.11	.68	.812±.004	.021	2.43±.15	.96	8.46±.33	2.09

[3] Victor, J., and Potter, J. S., *Brit. J. Exp. Path.*, 1935, **16**, 253.

metabolic differences between the 2 age groups and the various methods of transmission. The statistically significant differences are italicized.

TABLE III.
Metabolic Differences of Lymph Nodes of Old and Young Mice Inoculated with Line O.

Comparison of	Q_{O_2}		R.Q.		$Q^{O_2}_{CO_2}$		$Q^{N_2}_{CO_2}$	
	Diff.	Diff. / PE Diff.	Diff.	Diff. / PE Diff.	Diff.	Diff. / PE Diff.	Diff.	Diff. / PE Diff.
(2) — (1)	*.30*±.10	3.0	*.067*±.006	11.2	*.47*±.08	5.8	*1.27*±.40	3.2
(3) — (4)	*.50*±.15	3.3	*.086*±.005	17.2	.21±.22	1.0	*1.24*±.41	3.0
(1) — (4)	.16±.13	1.2	*.039*±.005	7.8	.25±.16	1.5	.40±.41	1.0
(2) — (3)	*.41*±.13	3.2	*.058*±.006	9.6	.01±.17	0	.43±.39	1.1

Two major conclusions may be drawn from these summaries. The first is that age has an effect upon the metabolism of transmitted leukemia cells. In older mice the R.Q. in the presence of glucose, Q_{O_2}, $Q^{O_2}_{CO_2}$, and $Q^{N_2}_{CO_2}$ are lower than in younger mice. If cells are transmitted through old mice and into younger the metabolism is higher with younger and *vice versa*. The effect of age is reversible. This reversibility of leukemia cell metabolism produced by host age is similar to that resulting from cell transmission through genetically different hosts.[4] The second point is that passage through the young and old mice (the center portion of the scheme) was associated with the development of 2 parallel lines that were distinctly different metabolically. This has been observed before[5] and is not necessarily correlated with passage through different age groups. Host age does not modify the inherent constitution of the leukemia cells but acts as a determining environmental factor on their metabolism.

[4] Victor, J., and Potter, J. S., *J. Exp. Med.*, 1934, **60**, 547.

[5] Victor, J., and Wintersteiner, M. R., *Am. J. Cancer*, 1934, **22**, 561.