

urine did not do so, even with large dosages and prolonged treatment. The only ovarian response is an increase in the number of corpora atretica of the small follicles only, and in the degree of hyalinization. The biological action of substances from these 2 sources is not the same when tested on the female *Macacus* monkey. These differences are more pronounced in the female than as seen in the male monkey (Engle), and add to the increasing mass of data that extracts of anterior pituitary and of human pregnancy urine are biologically different.

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Metabolic Differences Between Two Transmission Lines of Mouse Leukemia.*

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The experiments of Warburg¹ on the metabolic differences between tumors and normal tissues have stimulated similar investigations in leukemia. Although considerable data have accumulated relative to the metabolism of the cells in leukemia, many of the conclusions have been contradictory.

The following investigation has been undertaken as part of the program conducted in these laboratories in which the genetics, pathology and cytology of transmissible leukemia of mice have been reported by MacDowell, Richter and Potter.² The genetically controlled material developed in their studies is particularly suitable for metabolic experiments. The oxygen consumption and both aerobic and anaerobic glycolysis of normal lymph nodes and leuke-

* This investigation was supported by a grant from the Carnegie Corporation, and an appropriation from the Research Fund of Columbia University.

¹ Warburg, O., *Biochem. Z.*, 1924, **152**, 51.

² Richter, M. N., and MacDowell, E. C., *J. Exp. Med.*, 1930, **51**, 659. MacDowell, E. C., and Richter, M. N., *J. Cancer Research*, 1930, **14**, 434. Richter, M. N., and MacDowell, E. C., *J. Exp. Med.*, 1930, **15**, 823. MacDowell, E. C., and Richter, M. N., *Proc. Soc. Exp. Biol. and Med.*, 1931, **28**, 1012. MacDowell, E. C., and Richter, M. N., *Biol. Zentral.*, 1932, **52**, 266. Potter, J. S., and Richter, M. N., *Proc. Nat. Ac. Sc.*, 1932, **18**, 298. Potter, J. S., and Richter, M. N., *Arch. Path.*, 1933, in press.

mic lymph nodes of 2 distinct transmission lines, designated A and I, have been studied by one of us.

All animals were from strain C-58 in which 100% were susceptible to the transmitted disease. Line I killed the inoculated animals in 3 to 4 days, Line A in 6 to 8 days. Infiltration of the lymph nodes in Line I has been shown to be complete in 72 hours, while in Line A, 4 days.

Method. The animals were 6 to 8 weeks old. The experimental animals were of the same sex and almost invariably litter mates. Congested, hemorrhagic and necrotic glands were discarded. Four normal animals were sacrificed for each determination of the Q_{O_2} , $Q_{CO_2}^{O_2}$ and $Q_{CO_2}^{N_2}$ of the lymph nodes. In Line I, one or 2 animals were used; in Line A the lymph nodes of 3 mice were combined to obtain sufficient material. The quantity of tissue in each respirometer varied from 30 to 70 mg. moist weight. The nodes of Line I were used 3 days after inoculation, of Line A, 5 to 6 days after inoculation. The nodes were cut in strips about 2 to 3 mm. thick, while immersed in unbuffered or phosphate buffered Ringer's solution. The sliced tissue was placed in 1 to 2 cc. of solution in the respirometers, about 15 to 20 minutes after the animal was sacrificed.

Oxygen consumption and aerobic and anaerobic glycolysis were measured by the Warburg method² with the tissues in Ringer's solution in Fenn respirometers. The nodes were weighed at the end of the experiment after removal of excess fluid by blotting. All tissues were then fixed in Flemming's solution for cytological study. The moisture content of the tissues was estimated as 80% and the observed values were corrected by this factor.

Results. Table I is a summary of the experiments, showing for each series the range of metabolism, the mean, probable error and differences in metabolism, probable error of the difference and the ratio of the difference to the probable error. The differences are from 5.8 to 18 times the probable errors of the differences.

Not only are there striking differences between the metabolism of lymph nodes of normal and leukemic animals but also between those of the 2 different lines of transmissible leukemia. The O_2 consumption of nodes of Line A is greater than that of nodes of both Line I and normal. However, the aerobic glycolysis of Line I is almost 3 times as great as that of normal and Line A. Furthermore, the anaerobic glycolysis of lymph nodes of Line I is about 1.5 times as great as that of Line A and almost 3 times as great as that of normal.

TABLE I.
Metabolism of Lymph Nodes of Normal Mice and Those Inoculated with Transmissible Lymphatic Leukemias of Lines A and I.

| | No. Determinations | Range | Q O ₂ Mean | Diff. P.E. | Range | Q CO ₂ Mean | Diff. P.E. | Range | Q CO ₂ Mean | Diff. P.E. |
|---------------|--------------------|----------|-----------------------|------------|----------|------------------------|------------|-----------|------------------------|------------|
| Normal | 10 | 6.3-10.6 | 8.37±0.31 | | 1.7- 4.6 | 3.02±0.22 | | 4.8-12.7 | 7.9 ±0.57 | |
| Line I | 10 | 8.0- 9.1 | 8.59±0.01 | | 6.9-10.7 | 8.61±0.24 | | 15.0-27.2 | 20.2 ±0.85 | |
| Line A | 9 | 9.5-11.9 | 10.48±0.17 | | 1.5- 4.5 | 3.12±0.21 | | 8.1-18.3 | 14.12±0.6 | |
| Difference | | | | | | | | | | |
| Line I—Normal | | | None | | | 5.59±0.31 | 18 | | 12.34±1.03 | 12.0 |
| " A— | | | 2.11±0.35 | 6.0 | | None | | | 6.22±0.81 | 7.7 |
| " I—Line A | | | -1.89±0.19 | 10.0 | | 5.49±0.32 | 17 | | 6.12±1.03 | 5.8 |

These differences observed in different lines of lymphatic leukemia offer an indication of the causes of discrepancies occurring in the literature. Further investigation of this problem is necessary to explain the fundamental factors involved.