3. Human Strains. Rough colonies at pH 6.0 and 6.2. Smooth colonies at pH 6.4 and in a few instances at pH 6.6. These were also rounded, shiny and non-granular. Intermediate colonies from pH 6.8-7.4. These were similar in appearance to the bovine intermediate forms.

The data above indicate the dominant colony forms at the various pH values. When other colony forms appeared than those indicated, they were in the minority.

Total growth varied remarkably at the different pH values but showed no appreciable variation in the human, bovine or avian types. Growth was most vigorous at pH 6.0 and 6.2 and in general less vigorous the more alkaline the medium.

Animals have been inoculated with these colony variants derived from a freshly isolated human strain, a highly virulent bovine strain, and a bovine strain of very low virulence. From the latter experiments it has been found that the rough colonies are of least virulence, the smooth of greatest virulence, and the intermediate colonies are of intermediate virulence. Smooth colonies derived from the bovine strain of low virulence are apparently not more virulent than the undissociated culture from which they were derived.

Since all other variables were avoided, save that of hydrogen ion concentration of the standard medium, these experiments demonstrate the rôle which one factor may play in determining the colony morphology and virulence of tubercle bacilli.

8085 P

Histological Observations on Resistance to Transplantable Leukemia in Immunized Mice.

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Recently it has been demonstrated that immunization to transplantable lymphatic leukemia in mice can be actively induced by suitable injection of dilute doses of leukemic cells,[1] by injection of nor-

[1] MacDowell, E. C., Taylor, M. J., and Potter, J. S., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 84.

mal lymphoid cells,[2] and of embryo skin.[3] Naturally susceptible mice so treated are resistant to injections of normally lethal doses of leukemic cells at subsequent inoculations. This paper records the results of preliminary observations on the fate of malignant lymphoid cells inoculated into immunized mice.

A group of 19 mice of strain C58, immunized to line I transplantable lymphatic leukemia by dilute doses of line I cells as already described,[1] were killed at intervals following inoculation of a massive dose; 1 at 13½ hours, 1 at 1 day, 3 at 2 days, 7 at 3 days, 2 at 4 days, 1 at 5 days, 2 at 6 days, and 2 at 7 days. Unimmunized mice inoculated with this line die at 3½ to 4 days following inoculation. The development of lesions of this line of leukemic cells in hosts of strain C58 as previously described[4] forms a basis for comparison with the behavior of these leukemic cells in immunized hosts.

Examination of the tissues from the immunized animals shows that at first the inoculated cells continue to proliferate. Lesions may appear in the same areas as in unimmunized mice but never become so large. The percent of cells in division is low (0.3%-1.0%) as compared with active lesions at all stages in unimmunized mice (4%-9%) inoculated with line I.

Degeneration of the infiltrating cells usually takes place within the first 4 days. In only 2 animals out of the 14 killed after the second day were active lesions found without necrotic cells, but in these 2 animals necrotic lesions were also found, indicating that recovery was in progress. The process of degeneration of lesions apparently follows a regular sequence. The first indication is the degeneration of single cells in the peripheral margin of the lesion, and the degeneration spreads rapidly until chromophilic debris occupies the supporting stroma. At this time the host phagocytes appear and the debris promptly disappears. The remaining stroma may be invaded by host lymphoid cells, which appear at the site of the lesion for the first time at this stage, but soon disappear. In only one case was lymphoid hyperplasia associated with invasion by host cells. By the 6th and 7th day no evidence of the inoculation can be found.

The same stages of degeneration observed in actively immunized mice have also been observed in a naturally resistant strain, Sto-Li, following inoculation with line I.

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[2] Rhoads, C. P., and Miller, D. K., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 817.

[3] MacDowell, E. C., in press.

[4] Potter, J. S., and Richter, M. N., *Arch. Path.*, 1933, **15**, 198.

Immunity to transplantable lymphatic leukemia is apparently not the result of blockade or invasion of lesions by normal host lymphocytes as has been supposed in resistance to other types of neoplasms,[5] since the injected cells are necrotic before the mobilization of host cells.

8086 P

Influence of Thyroid Administration on Creatin Metabolism in Myxedema of Adults.

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Little is known of the creatin metabolism of adult myxedema other than the absence of spontaneous creatinuria. In children with cretinism or hypothyroidism, the physiological creatinuria of childhood is absent.[1, 2] When thyroid substance is given to such children, large amounts of creatin appear in the urine.[1, 2] This effect has been interpreted as a restoration of the normal creatinuria of childhood. It is not known, however, how long the creatinuria persists with continued administration of thyroid substance in amounts sufficient to maintain a normal basal metabolism.

We have studied the creatin metabolism of 2 typical cases of spontaneous adult myxedema. Their diet was creatin-creatinin-free, and adequate in calories and protein. The ability to retain ingested creatin (1.32 gm.) was tested from time to time. After a control period, thyroid substance was administered in amounts sufficient to restore and maintain a normal basal metabolism. The usual improvement in signs and symptoms took place. Six cases of myxedema following total ablation of the thyroid* were studied in the same way, except that no thyroid substance was given. Our findings in spontaneous myxedema are given in Table I and Chart 1.

Results. In agreement with other workers, we found no creatinuria in spontaneous adult myxedema. Creatinuria was also ab-

[5] Murphy, J. B., Monographs of the Rockefeller Inst. for Med. Res., 21, 1926. Lumsden, Thomas, *Am. J. Cancer*, 1931, **15**, 563.

[1] Beumer, H., and Iseke, C., *Berlin. Klin. Wchnschr.*, 1920, **57**, 178.

[2] Poncher, H. G., Visscher, M. B., and Woodward, H., *J. Am. Med. Assn.*, 1934, **102**, 1132.

* We are indebted to Dr. Herrman L. Blumgart of Boston for these cases.