were given 200 mg of Prontylin† in 10 cc physiological saline daily by intraäbdominal injection. It was found that a solution of this strength could be prepared by heating the salt solution, dissolving the drug, and cooling to body-temperature. Injections were then made immediately before recrystallization took place. This dose was given daily for 23 days, at which time it was increased to 250 mg in 12.5 cc saline solution. The latter dose was given daily for 7 days, when treatment was discontinued because the animals were not benefitted by it.

The first death in the control group occurred on the 24th day and the last on the 51st day following inoculation. In the treated group the first death occurred on the 12th and the last on the 49th day. The mean survival time for the 2 groups was $34.1 \pm 1.9$ and $30.8 \pm 1.6$ days respectively. This difference is not significant. Gross necropsy-findings in the 2 groups were remarkably similar.

The difference in the methods we have used and those referred to above[1] are fourfold. We have used fewer organisms and have inoculated intracerebrally rather than subcutaneously; we have given the Prontylin intraäbdominally in solution rather than by mouth; and lastly, we have relied upon survival-time to determine the effect. Since this drug is effective in certain other bacterial infections of the meninges, we do not consider that the route of inoculation invalidates this experiment. Moreover, survival-time after intracerebral inoculation of tubercle bacilli can be influenced by other means to be reported later. However, the possibility cannot be excluded that Prontylin may be more effective by mouth than by parenteral injection.

*Conclusion.* Under the conditions of our experiments, Prontylin exerted no beneficial effect in experimental tuberculosis.

**9942 P**

## Effect of Age of the Host on Resistance to Tuberculous Infection.

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In order to standardize procedures for virulence-tests, or tests on immunization, it is necessary to know the possible sources of varia-

† *p*-amino-phenyl-sulfonamide, supplied by Winthrop Chemical Company, Inc.

tion and to control them insofar as it is possible. The experiments to be discussed were done to ascertain whether or not young guinea pigs were more susceptible to experimental tuberculosis than older, mature animals.

Three strains of tubercle bacilli were used in the experiments: a bovine strain 39, isolated by the late Dr. Theobald Smith, and 2 lines of the human type strain H-37, one moderately virulent, the other highly virulent. Albino guinea pigs of both sexes were used but males were caged separately from females. All animals were inoculated intracerebrally[1] under anesthesia induced by the intraäbdominal injection of 0.5% solution of Seconal,* the dose being the equivalent of 20 mg per kg. All animals were allowed to succumb to the infection. A necropsy was performed on each animal at death in order to make pathological surveys and detect any possible intercurrent factors.

In the first experiment, 3 female guinea pigs weighing 840 to 1060 g and 4 immature males weighing from 120 to 180 g were inoculated intracerebrally with 0.001 mg of the bovine strain 39. In addition, one female and 2 male guinea pigs weighing from 680 to 860 g, 2 males and 2 females weighing 100 to 140 g were inoculated intracerebrally with 0.001 mg of the moderately virulent line of the human strain H-37. The mean survival for those receiving the bovine organisms was 21.5 days for the old and 27.25 days for the younger animals. Among those receiving the H-37 the average survival was 31.3 days for the old animals and 32.6 days for the young animals. Two animals in this experiment died from complicating non-tuberculous pneumonia and were excluded from consideration.

In a second experiment 3 females and 2 males weighing 860 to 1040 g constituted one group. Five male guinea pigs weighing 380 to 480 g constituted a second group, and 5 females weighing 100 to 160 g constituted a third group, so that the experiment included old, middle-aged, and young animals. Each animal of the 3 groups was inoculated intracerebrally with 0.00001 mg of the highly virulent line of human tubercle bacilli, strain H-37. All animals received the same dose of the same suspension of the organisms within the same hour. The mean survival for the old animals was $23.8 \pm 0.80$ days; for the middle-aged group, the mean was $27.6 \pm 1.10$ days, and for the young it was $35.8 \pm 0.78$ days. The differences

[1] Smithburn, K. C., *J. Exp. Med.*, 1936, **64**, 771.

* Sodium propyl-methyl-carbinyl allyl barbiturate, Lilly, supplied by Eli Lilly and Company, through Dr. G. F. Kempf, Indianapolis City Hospital.

were compared by statistical analysis and proved to be significant. The differences in mean survival of the old and middle-aged group, 3.8 days, is 2.8 times the probable error of that difference, and the odds against occurrence by chance are about 15 to 1. The difference in mean survival of the middle-aged and young groups, 8.2 days, is 6.1 times its probable error and the odds against chance occurrence are very high. More striking still, the difference in mean survival of the old and young groups, 12.0 days, is 10.8 times the probable error of the difference and the odds against occurrence by chance are extremely high.

The differences noted cannot be attributed to sexual differences in expectancy as pointed out by Berg[2] since the experiments were terminated quickly by the acuity of the disease; furthermore, the young animals of the second experiment, which might have been expected by Berg's criteria, to die the earlier, proved to be the more resistant. It should be emphasized also that the inoculating dose per animal was the same in mass. Calculating on the basis of mg of bacteria per kg of body weight, the young animals received 7.7 times the dose given to the old and 3.3 times the dose given to the middle-aged group. Since all other conditions of the experiment were the same in the 3 groups, the differences noted must have been due to variations in resistance with age.

*Conclusion.* Resistance to tuberculosis, as measured by survival-time of guinea pigs after intracerebral inoculation, varies with age. Young animals are the more resistant, and susceptibility increases progressively with age.

## 9943

## Hypoglycemic Response of Patients Using Protamine Zinc Insulin to Induced Hyperglycemia.

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Some of the difficulties encountered in treating diabetes could be attributed to rapidly fluctuating blood sugar levels. The slow acceptance of protamine zinc insulin by the clinician was, in part, due to the occurrence of hypoglycemia episodes. They can be differentiated into two groups, the nocturnal, and the post-prandial. The

2 Berg, W. N., *Am. Rev. Tuberc.*, 1938, **37**, 259.