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Nicotine Tolerance in the White Rat.

C. H. THIENES.

*From the Department of Pharmacology, University of Oregon Medical School,  
Portland, Oregon.*

The minimal effective dose (M.E.D.) of nicotine for white rats of both sexes, from 29 to 33 days old, was 0.3 mg. per kilo body weight. This dose was sufficient to cause slight but definite weakness of the hind legs. After determining the M.E.D., one-half of each of 3 litters were injected twice daily with 2 to 3 times the M.E.D., producing symptoms ranging from instability to convulsions and prostration. At intervals of 3 and 9 weeks following the first injections, after a rest day of no injections, all rats were tested for the M.E.D. Whereas the controls, 10 in number (injected twice daily with salt solution), responded each time to 0.3-0.4 mg. nicotine per kilo body weight, the test rats, 13 in number, showed a definite decrease in susceptibility, in that at the end of 3 weeks, the M.E.D. averaged 0.65 mg. nicotine, and at the end of 9 weeks, 0.85 mg. per kilo body weight. This was considered to be evidence of an acquired nicotine tolerance.

An interesting phenomenon of "acute tolerance" was also observed. That is, the second injection of the day caused much milder symptoms than the first injection. Although not yet well worked out, it seems that the optimal interval between injections for demonstrating this phenomenon is from 2 to 4 hours.