observed among males exposed to the other 2 test compounds while none appeared in either of the control groups. The data demonstrate that a minute amount of N-OH-FAA had a potent tumorigenic effect in the liver when tested in infant male mice.

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Insulin Hypoglycemia Enhanced by Beta Adrenergic Blockade.* (31066)

SANFORD O. BYERS AND MEYER FRIEDMAN

Harold Brunn Institute, Mount Zion Hospital and Medical Center, San Francisco, Calif.

"Inderal" (AY 64043,† I.C.I.‡ 45,520, propranolol) is 1-isopropylamino-3-(1naphthyloxy)-2-propranol hydrochloride and is an adrenergic beta receptor antagonist now undergoing clinical trial (1). In connection with work on triglyceride transport in the rat(2) we had occasion to administer "Inderal" together with insulin. The ensuing hypoglycemia was much more severe than when either agent was administered alone. "Inderal" is but one of a number of compounds of similar pharmacological properties now coming into use and which may well be administered to patients also taking insulin. Our data are reported in the hope that it may alert physicians to the possibility of an undesirably low hypoglycemia following production of beta adrenergic blockade in diabetic patients.

Male rats of the Long-Evans strain, weighing about 300 g, were starved for 14 hours after which they received 3 ml or corn oil *per os*. They then were divided into 6 groups. Group I (10 rats) served as controls and were untreated. Group II (10 rats) received 50 mg of propranol *per os*. Group III (5 rats received 0.5 unit of regular insulin intramuscularly. Group IV (5 rats) received 0.5 unit of insulin and 50 mg of propranolol. Group V received 1.0 unit of regular insulin. Group VI received 1.0 unit of insulin and 50 mg of propranolol *per os*. The rats of all groups were bled 6 hours after treatment. Some of these same rats also were bled either 1 or 3 hours after treatment. Glucose levels in heparinized plasma from the blood samples were determined using glucose oxidase (3).

The results (Table I) indicated that although administration of propranolol alone did not significantly alter the plasma glucose level of the rat, when it was administered together with insulin, it markedly intensified the hypoglycemic effect of the latter. Indeed when the blocking agent was administered with 1 unit of insulin, the average plasma

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† Ayerst Laboratories, New York.

‡ Imperial Chemical Industries, Cheshire, England.

TABLE I. Plasma Glucose (mg/100 ml)* After Treatment

	1 hr	3 hr	6 hr
(1) Untreated	170 ± 8	167 ± 10†	161 ± 8
(2) Propranolol	175 ± 10	200 ± 14†	185 ± 8
(3) Insulin (0.5) unit	60 ± 4	—	115 ± 11
(4) Propranolol + insulin (0.5) unit	46 ± 9	—	78 ± 24
(5) Insulin (1) unit	—	56 ± 12	115 ± 4
(6) Propranolol + insulin (1) unit	—	8 ± 2	all dead

* Values are means ± standard error of mean.
† Only 5 of the 10 rats were bled at this time interval.

glucose sank to 8 mg/100 ml at the 3-hour interval and shortly thereafter all animals exhibited typical hypoglycemic convulsions and died. These results are probably due to the inhibition by propranolol of the usual epinephrine-induced glycolytic reaction following insulin administration(4,5).

Summary. "Inderal" (Ayerst 64043, Imperial Chemical Industries 45,520, propranolol) an adrenergic beta receptor antagonist, acts synergistically with insulin in the rat to induce a hypoglycemia much more severe than that resulting from insulin alone. This synergism may possibly be of clinical significance.

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Exacerbation and Transformation of Allergic Encephalomyelitis by Pertussis Vaccine.* (31067)

SEYMOUR LEVINE AND EUGENE J. WENK
Pathology Department, New York Medical College, Center for Chronic Disease, Bird S. Coler Hospital Division, Welfare Island, New York City

Injection of central nervous system (CNS) tissue in animals usually elicits a single attack of experimental allergic encephalomyelitis (EAE), but relapses occur spontaneously on occasion or can be induced by reinjection of CNS antigen(1,2). Demyelinating diseases like multiple sclerosis are characterized by relapses. To simulate more closely such a clinical course, exacerbations and relapses were induced in rats with EAE by injection of pertussis vaccine. For the first time relapses have been induced at will without repeating the primary immunization against neural antigen. Of especial interest was the observation that the primary attack and the exacerbation differed in histologic character and could be differentiated under the microscope.

Methods. EAE was induced in 75 female rats of the highly susceptible Lewis strain (Microbiological Associates, Inc.) by injection of an aqueous homogenate of 200 mg guinea pig spinal cord (without any adjuvant) into 5 pads on the sole of the right hind foot(3). All injections were given under light ether anesthesia. Thirty-seven of the rats developed clinical signs of EAE after 8-13 days (limp tail, weakness). Within 2 days after the onset of symptoms they were treated by one of the following: injection of pertussis vaccine concentrate (either unheated or heated to 80°C for 30 minutes), typhoid vaccine concentrate, or no treatment, according to the schedule and dose listed in

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