hydroxysteroid dehydrogenases (E.C. 1.1.1.51) in fetal adrenal explants. Less tritiated dehydroepiandrosterone accumulated in two of the experimental vessels, and in all vessels more of the Δ 4-3 ketone steroids were formed. Adrenal explants exposed to testis RNA also formed more androgen (androstenedione plus testosterone) than control explants did. This effect may be due in part to the increased activity of the 3β-hydroxysteroid dehydrogenase; however, examination of the products of progesterone-4-^{14}C (Table 3) reveals that synthesis of testosterone-^{14}C was increased in all three vessels. There was no effect of testis RNA on the synthesis of glucocorticoids (corticosterone and cortisol) from progesterone. Thus, in these experiments adrenal explants from human fetuses shifted to a pattern of steroid synthesis that more closely resembled the source of the RNA to which they had been exposed.

We have already shown (*1*) that ovaries and adrenals of rats and mice are susceptible to the influence of ribonucleic acid introduced into the organ-culture medium of the explants. We have extended these observations to the testis and adrenal of the human fetus. Our experiments with two isotopically labeled substrates suggest that the influence of RNA is on several enzymes and not merely on a single one.

These results must be interpreted with caution because the contamination of the RNA with a small amount of protein cannot be ruled out. Experiments with hydrolyzed RNA [20 μg of ribonuclease (from Worthington) per milligram of RNA] and with RNA extracted from kidney suggest that intact RNA from a steroid-producing gland is required for the biologic effects previously noted. However, our experiments do not provide conclusive evidence of template activity of the RNA added to the culture medium. Both testes and adrenals can synthesize most of the steroid hormones; therefore, a shift in pattern of steroid metabolism may be mediated by influences which may not necessarily involve the function of an RNA template.

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Tetraethylammonium Chloride as an Antidote for Certain Insecticides in Mice

Abstract. *In tests on mice, tetraethylammonium chloride (TEAC) was superior to atropine sulfate as an antidote for some carbamate insecticides and nicotine; it did not produce the traumatic and sometimes fatal reactions caused by atropine sulfate, although injections of the two antidotes provided equal protection against lethal oral doses of the carbamates Zectran, NIA-10242, and Lannate. The effects of TEAC were not evaluated against the carbamates Sevin and Baygon because acute oral toxicity values could not be determined. Results with Matacil were inconclusive. Tetraethylammonium chloride was not an effective antidote against the organophosphate Parathion, but its use fully eliminates the effects of nicotine intoxication.*

The carbamate insecticides Sevin (*1*) (1-naphthyl methylcarbamate) and Zectran (*2*) (4-dimethylamino-3,5-xylyl methylcarbamate) inhibit a chlorinesterase in the blood serum of mice (*3*). We tried to determine the value of tetraethylammonium chloride (TEAC) as an antidote for mice treated with carbamates.

Pellets of pesticides were made with a hydraulic press, and lethal doses were fed orally to 9-week-old female Swiss-strain mice weighing 25 g. Ten minutes after such feeding, TEAC at 20 mg/kg was injected intraperitoneally, intravenously, or intramuscularly. The antidotal effects of TEAC were ascertained after intravenous injection. Ten mice were used in each series of tests, and the surviving animals were killed and autopsied 30 days after treatment.

Within 10 to 30 minutes of receiving a lethal dose of Zectran [LD_{50} (lethal dose, 50 percent effective), 30 to 50 mg/kg], mice exhibited characteristic response: tachypnea, fasciculation of the back, excessive salivation, acute conjunctivitis, gasping, convulsions, and death. Although the survival rates of Zectran mice subsequently treated with either TEAC or atropine sulfate were comparable, those treated with atropine showed symptoms attributable to either atropine or Zectran. However, mice subsequently treated with TEAC not only were free from the Zectran syndrome, but were quiet and relaxed.

The control mice treated with TEAC only were quiet and relaxed for about 1 hour after injection and then resumed normal activity. The control mice treated with atropine sulfate alone were irritable and hyperactive, showing an accelerated respiration rate for at least 4 hours after treatment. These effects made it difficult to establish a satisfactory antidotal dosage. The dosage of atropine sulfate was 8 or 80 mg/kg orally; 8 or 80 mg/kg intramuscularly; or 4, 8, 40, or 80 mg/kg intraperitoneally. Whether TEAC was injected intramuscularly or intraperitoneally, there was no apparent difference in its effect as an antidote on mice fed Zectran at 80, 160, or 320 mg/kg.

Sodium barbital alone gave no protection against a lethal oral dose of Zectran, nor did it enhance or antagonize the effect of TEAC. Tetramethylammonium hydroxide, betaine hydrochloride, hyoscyamine sulfate, 3,3-dimethyl butyl acetate, ethyl acetoacetate, and isoamyl isovalerate were each ineffective as antidotes after a lethal oral dose of Zectran.

A lethal oral dose of the carbamate insecticide NIA-10242 (*4*) (2-3-dihydro-2,2-dimethyl, 7-benzofuranyl *N*-methylcarbamate) caused in mice symptoms similar to those of Zectran; death occurred within 10 to 15 minutes. Mice fed a lethal dose of NIA-10242 and later treated with TEAC survived; they showed occasional slight tremors and appeared quiet but ill for about 3 hours.

Mice fed a lethal dose of the carbamate Lannate (*5*) [*S*-methyl *N*-(methylcarbamoyloxy)thioacetimidate] showed symptoms resembling those in mice fed Zectran or NIA-10242. Lannate, however, was unlike NIA-10242 in that the antidotal effect of TEAC was immediate: the animals resumed normal activity within 10 minutes of injection.

The antidotal effect of TEAC on mice fed Sevin could not be determined since the mice tolerated an acute oral dosage of 2.0 g/kg. Baygon (*6*) (2-isopropoxyphenyl methylcarbamate) likewise was not a satisfactory test insecti-

cide in mice; determination of the LD_{50} value was hindered by very erratic response.

Matacil (*7*) (4-dimethylamino-3-tolyl methylcarbamate) produced symptoms different from those of other carbamates; eight of the ten mice fed 130 to 200 mg/kg became lethargic and stuporous and died 12 to 20 hours later; because of the prolonged symptoms and delayed death, the effectiveness of TEAC as an antidote could not be ascertained. The time at which the TEAC is administered as a treatment may be critical (*8*).

Mice fed a lethal dose of the noncarbamate Parathion (*9*) (*O,O*-diethyl-*O*-*p*-nitrophenyl phosphorothioate) died in convulsions in 10 to 15 minutes, with or without TEAC injected as an antidote. After treatment with a lethal dose (50 mg/kg) of the noncarbamate nicotine, mice injected with TEAC at 20 mg/kg did not show the typical nicotine syndrome of convulsions, curare-like paralysis, and death within 10 minutes.

Tetraethylammonium chloride appeared to be a safer and more effective antidote than atropine sulfate for some insecticide intoxication; TEAC blocks transmission at autonomic ganglia, and the effects are mutually antagonistic to adrenergic and cholinergic substances (*10*); it shows promise as an antidote because of its therapeutic effect and because its side effects were less than those of atropine sulfate at the concentrations tested.

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Creatine Kinase and Aldolase in Serum: Abnormality Common to Acute Psychoses

Abstract. *Activity of creatine kinase and aldolase in serum increased in 14 of 16 patients with recent onset of a psychotic reaction, and in five of six patients treated with psychotomimetic drugs. There was either no increase of these enzymes or a slight increase in severely agitated (or depressed) nonpsychotic hospitalized patients and chronic psychotic patients. The increase of the enzymes preceded the onset of the acute psychotic symptoms in at least three cases, was highest during the first 2 weeks of a psychotic episode, and sometimes recurred throughout the illness, particularly at times of stress. The creatine kinase in the serum is primarily of the muscle type.*

Incidental to a study of creatine kinase (CPK) (E.C. 2.7.3.2) in the serum in neurologic disorders, Schiavone and Kaldor found that the activity of the enzyme in the serum of nine of 24 schizophrenic patients had increased (*1*). In investigating changes in the serum during treatment with psychotropic drugs, Bengzon *et al.* found that in 30 of 60 acutely psychotic patients the activity of CPK and aldolase (E.C. 4.1.2.7) was increased before treatment. After the patients were treated with phenothiazines, the activity returned to normal within 1 week in females and within 4 weeks in males (*2*). I now report on the incidence of increased activity of these enzymes in the serum of schizophrenic and other psychiatric patients, and the results of a study on the sources of the increase.

This study was made on 16 acutely psychotic patients, 14 chronically psychotic patients, and 11 patients who were not psychotic by clinical evaluation or psychological testing but who required psychiatric hospitalization because of severe agitation, anxiety, or depression. The clinical status of the patients and other clinical data apart from biochemical data were ascertained (*3*). The CPK and aldolase were determined spectrophotometrically by a series of coupled enzyme reactions resulting in the reduction of nicotinamide nucleotides (*4*). In our laboratory, normal amounts of CPK in serum are 10 to 50 I.U./liter for men and 10 to 40 I.U./liter for women, whereas those of aldolase are 200 to 400 μmole ml^{-1} hr^{-1}.

In nine of 11 acute schizophrenic patients, a significant increase in activity of CPK and aldolase in serum was found at some phase of their clinical course (Table 1) (*5*). Four patients suffering from the other acute psychoses, including three manic-depressive patients in the manic phase and one patient with acute psychotic depression, also exhibited greatly increased activity of these enzymes. Furthermore, one patient with periodic catatonia had abnormally high activity of these enzymes during the first week of a catatonic episode, whereas previously it was normal (*6*).

Six of the 16 acutely psychotic patients were quite disturbed at the time of admission, and their serum had increased enzyme activity which returned gradually to normal, usually within 10 days or less. One patient, though admitted to the hospital in a distinctly psychotic state 3 days after the abrupt onset of his symptoms, had normal activity of CPK and aldolase at that time, but it increased dramatically 3 days later as his clinical condition temporarily worsened. Seven of the patients were first studied in a relatively quiescent phase of their illness, and their serums initially had normal enzyme activity. These patients had a recurrence or exacerbation of an acute psychotic state, at which time both enzymes increased sharply. With three of these patients, blood samples taken prior to the first clinical evidence of recurrent decompensation established that the enzyme increase preceded the first clinical detection of the psychotic state by 8 days in one case and by 4 days and 2 days in the others. In one of these patients, the enzyme increase began at the time of the first home visit in 2 months, and in the second patient it began when he was given community privileges and urged to find employment. In general, the increase in activity of CPK and aldolase in the serum was greatest before or at the outset of one of these recurrent episodes and gradually returned to normal or near normal in 2 to 5 weeks. No differences were noted between enzyme activity in males and females. However, transient increase in this activity recurred in some patients throughout their hospitalization, even though they were no longer considered to be psychotic. This was particularly true of the period before discharge when the patients were experiencing the stress of making major readjustments to their life situations. One of the patients with normal enzyme activity throughout a lengthy and stormy