lowing fatty meals or administration of intravenous fat emulsions. This observation demonstrates a further similarity in lipid metabolism between avian and mammalian erythrocytes.

The data presented indicate that the lipid content of the avian erythrocyte, like the mammalian cell, remains relatively constant and unaffected by plasma lipid levels.

Summary. Data are presented on the composition of chick plasma and erythrocyte lipids. The erythrocyte lipids differ from plasma lipids in that 96% of the cholesterol is present as the free form, lipid phosphorus is over twice as high as the plasma level, and the glyceride level is approximately one-third that of plasma. The total lipid level of red cells (mg/100 ml) was also found to be higher than that of plasma. A lack of correlation between erythrocyte and plasma levels of cholesterol and glycerides was noted, indicating that erythrocyte lipid levels are independent of plasma concentration. The similarities between avian and mammalian erythrocyte lipids are discussed.

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Effect of Repeated Oral Administration of Monoamine Oxidase Inhibitors On Rat Brain Amines. (27198)

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Green and Erickson(1) recently reported that changes in rat brain serotonin (5 HT) concentration produced by a single oral administration of either trans-2-phenylcyclopropylamine hydrochloride (tranylcypromine) or 1-isonicotinyl-2-isopropyl hydrazine phosphate (iproniazid) closely followed the effect of the drug upon brain monoamine oxidase (MAO) activity; *i.e.,* 5HT concentration continued to rise during the time that MAO activity decreased and was completely inhibited, and then returned to normal at about the same rate that the normal enzyme activity was restored.

The time course of changes in brain norepinephrine (NE) concentration induced by iproniazid also reflected the effect of the drug upon MAO activity. Following oral administration of tranylcypromine, however, brain NE concentration reached a peak in about 5 hours then slowly fell during the next 11 hours, while MAO activity remained completely inhibited. This disparity between inhibition of MAO and decrease in elevated NE concentration suggested that an alternate metabolic pathway, in addition to that of MAO, may operate in the rat brain for the degradation of NE, although conclusive evidence in support of this is lacking(2).

The purpose of the present study was to

determine effect of prolonged inhibition of rat brain MAO upon brain amine concentrations.

Procedure and methods. Male albino rats, Wistar strain, weighing between 125 and 150 g and housed 3 in a cage were used. Tranylcypromine and iproniazid were dissolved in water and administered orally twice a day, 8 hours between daily doses, for the indicated number of days. Doses of drugs refer to free base content. Animals given iproniazid were sacrificed 16 hours after last dose; animals given tranylcypromine were sacrificed 5 hours after morning dose of following day for NE analysis, and 7 hours for 5HT analysis. In all experiments a similar number of normal rats were administered water. Single brains were used for each analysis. NE analysis was performed by the method of Shore and Olin(3) as modified by Green and Erickson(4); 5HT analysis by the method of Bogdanski *et al.*(5).

Spontaneous motor activity of rats was measured in a motor activity-light chamber.

Results. (Fig. 1). Repeated daily oral administrations of tranylcypromine (5 mg/kg, b.i.d.) or of iproniazid (50 and 100 mg/kg, b.i.d.) to rats for 3 to 10 days resulted in cumulative increases in brain 5HT concentration of from 2 to 4 times that produced by a single administration of the drug. NE concentration was not appreciably different from that following a single administration of drug. The rats showed no overt pharmacologic responses. No significant or consistent effect upon the motor activity pattern of the drug-treated rats compared to untreated rats was observed.

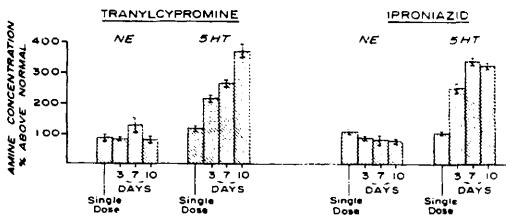

FIG. 1. Effect of repeated daily administrations of tranylcypromine and iproniazid on rat brain norepinephrine (NE) and serotonin (5HT) concentrations. All values are avg of 6 experiments. Vertical lines with cross bars represent stand. errors of means. Tranylcypromine: oral, 5 mg/kg, b.i.d., 8 hr between daily doses, for indicated number of days. On the following day rats were sacrificed 5 hr after morning dose for NE analysis and 7 hr for 5HT analysis. Iproniazid: oral, 50 mg/kg, b.i.d., 8 hr between daily doses. On following day rats were sacrificed 16 hr after last dose. The single dose was 100 mg/kg. For the 3-day experiment rats were given 100 mg/kg, b.i.d. In all experiments the same number of rats were administered water and used as controls. Normal control values: NE, 0.250 μg/g; 5HT, 0.474 μg/g.

Discussion. The cumulative increase of rat brain 5HT concentration following repeated daily administration of MAO inhibitor was consistent with previous observations (1) that changes in rat brain 5HT concentration reflected changes in activity of the brain enzyme. It further emphasized the predominant role that MAO plays in the metabolism of rat brain 5HT. The failure of brain NE concentration to exceed the level attained after a single administration of MAO inhibitor suggests that a mechanism exists whereby the brain protects itself against excessive accumulation of NE. Whether this mechanism is an alternate metabolic pathway, in addition to the MAO system, which becomes dominant when MAO is inhibited, or operates to control the rate of synthesis of NE by negative feed back, is not known. Evidence in favor of catechol-O-methyl transferase playing an important role in the metabolism of rat brain NE is lacking(2). Indeed, in our laboratory we failed to detect the presence of normetanephrine, the product resulting from action of the enzyme upon NE, in brains of rats after repeated administrations of tranylcypromine. Axelrod(6), however, reported the presence of this compound in brains of rats after chronic treatment with iproniazid.

The absence of any significant or consistent effect upon the motor activity pattern of chronically treated rats agrees with previous observations(1) of the failure of a single large administration of either MAO inhibitor to elicit overt pharmacologic responses.

Spector *et al.*(7,8) observed that daily subcutaneous doses of iproniazid to rabbits elicited marked increase in spontaneous motor activity which, they suggested, was temporally related to the rise in brain NE concentration, but not to the blocking of MAO activity or to the elevation of brain 5HT concentration.

Summary. Repeated daily oral administrations of tranylcypromine (trans-2-phenylcyclopropylamine) (5 mg/kg, b.i.d.) or of iproniazid (1-isonicotinyl-2-isopropyl hydrazine) (50 and 100 mg/kg, b.i.d.) to male albino rats, Wistar strain, for periods of from 3 to 10 days resulted in cumulative increases in brain serotonin concentration of from 2 to 4 times that produced by a single administration of the drug. The increase in norepinephrine concentration was not appreciably different from that following a single administration of the drug. No significant or consistent effect upon the spontaneous motor activity of the rats was observed.

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Relationship Between Hog Cholera Virus and Virus Diarrhea Virus of Cattle.* (27199)

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Use of a cowpox virus vaccine to protect people against smallpox virus by Jenner(1) was the first example of using one living virus to prevent illness caused by another. Since then many vaccines for man and for animals have been developed, but always by use of homologous virus that has been either inactivated or altered in virulence. Later virologists have considered cowpox virus to be a variant type of smallpox virus; the 2 have been reported to be immunologically related because serum from vaccinated individuals neutralized smallpox virus and serum of alastrim patients neutralized the viruses of vaccinia, of cowpox and of variola(2,3).

The idea of using different viruses as Jenner did has not been generally explored. Recent studies have shown that animals can be protected by viruses immunologically distinct, not by producing measurable neutralizing antibodies, but by inducing neutralizing antibodies to form more quickly (secondary response), thereby giving protection. Because this protection has no direct immunological basis, it is termed resistance. This concept of resistance is presented here.

Materials and methods. Viruses used. Two strains of cattle VD (virus diarrhea) virus were used for inoculation of pigs. One of these, Oregon C24V, cytopathogenic for tissue-cultured bovine kidney cells, was used for neutralization tests. The other, New York 1, that was not cytopathogenic, was maintained in spleen from an infected calf. The fully virulent HC (hog cholera) virus designated strain A, was maintained in spleen from an infected pig. A tissue-cultured derivative that was cytopathogenic was used for neutralization tests.

Animals. Litters of pigs were obtained when they were 8 weeks of age from a disease-free herd maintained by the Institute. Each litter was placed in an isolation unit. One week later one-half of the first litter of 4 pigs was inoculated intramuscularly, each with 1 ml of a 10% spleen emulsion prepared from a calf infected with New York 1 VD virus; the remainder of the litter was left uninoculated as controls. For the second litter of 6 pigs, one-third of the pigs of the litter was given New York 1 VD virus, one-third was

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