cottonseed oil fed was 3%, these data are not in conflict with the observations reported herein. In fact, the disproportionately increased dienoic acid deposition obtained with the highest level (Fig. 3) suggests a similar upward curvilinear trend. Mead *et al.*(7) have shown that a large proportion of the ingested linoleic acid is rapidly oxidized. Conversely, from the prolonged time required for the depletion of linoleic acid from animal tissues, that deposited is relatively metabolically inert.

It would seem probable that as the dietary level of dienoic acids changes the ratio of the amount oxidized to that deposited also changes. The data presented herein coupled with that of Ellis *et al.*(6) may be interpreted to indicate at least 3 such changes. At dietary intakes up to about 0.2% dienoic acids, the ratio of dienoic acids oxidized to that deposited remains constant. Between about 0.2%-0.8% a larger proportion of the ingested dienoic acids is oxidized, and as the levels increase above 0.8%, an increasingly larger fraction of the ingested dienoic acids is deposited. The foregoing considerations are, of course, largely speculatory and considerably more evidence is required for confirmation.

Summary. (1) Ether extracted soybean oil meal has been found to contain sufficient residual dienoic acids to account for the previously observed increased carcass fat dienoic acids of animals that ingest the meal. (2) Studies were conducted, with mice, on the carcass-fat levels of dienoic acids obtained as the dietary-dienoic-acid levels varied from 0 to 1.6%. Between the dietary levels of 0.1% and 0.8% dienoic acids, a curvilinear response curve was obtained and became linear when the logarithm of dietary intake was plotted against the logarithm of carcass fat level. At a dietary level of 1.6% dienoic acids, a disproportionately higher dienoic acid level was found in the carcass fat.

The vitamins used in the purified diets were kindly supplied by Merck and Co., Rahway, N. J.

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Effect of Dibenamine and Pyribenzamine on Hypothermia of Chlorpromazine. (23655)

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Tranquilizing drugs such as reserpine and chlorpromazine injected into an animal are reported to release a variety of substances which independently have a diversity of actions. These substances are 5 hydroxytryptamine(1), some sympathetic neurohumoral agent(2,3,4), and possibly histamine.* All these substances have a common effect which is that of lowering the body temperature(5,6,7,8). The purpose of this study was to determine the effect on body temperature of certain drugs which are known antagonists to these products released by chlorpromazine. The substances used were dibenamine, which antagonizes the edema producing effect of 5-

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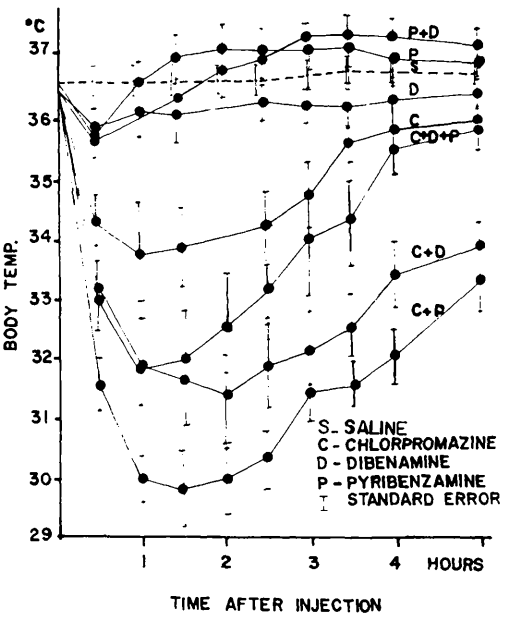

FIG. 1. Effect of intraperitoneal injections of chlorpromazine (8.5 mg/kg), dibenamine (21 mg/kg) and pyribenzamine (10.5 mg/kg) on body temperature of rats. (The standard error at 0 time is between 0.1 and 0.2°C for all groups.)

hydroxytryptamine(9) and has well known potent adrenergic blocking properties, and pyribenzamine, one of the antihistamines.

Methods. Eight groups of 6 white male rats, weighing 120 g, were used. These groups, which were all injected at the same time and on the same day, were treated respectively with: 1) chlorpromazine (8.5 mg/kg) (CPZ); 2) CPZ (8.5 mg/kg) + dibenamine (21 mg/kg); 3) CPZ (8.5 mg/kg) + pyribenzamine (10.5 mg/kg; 4) CPZ + dibenamine (21 mg/kg) + pyribenzamine (10.5 mg/kg); 5) dibenamine (21 mg/kg); 6) pyribenzamine (10.5 mg/kg); 7) dibenamine (21 mg/kg) + pyribenzamine (10.5 mg/kg) and 8) saline (8.5 mg/kg). Each drug was injected intraperitoneally and prepared in such concentration that the injected volume was 0.1 ml. The following fluid was used to dissolve 100 mg of dibenamine: 24.2 ml ethanol. 24.2 propylene glycol ml and 0.1 ml concn. HCl. Prior to its use, this solution was diluted with saline to the proper concentration. Body temperature was measured with a thermocouple inserted through the anus to a depth of 40 mm. The animals were kept in a room maintained at 72° F.

Results. Fig. 1 shows that dibenamine and pyribenzamine injected alone or simultaneously will cause a drop of approximately 1°C in body temperature. A reversal of this effect is observed 1 hour after injection although the dibenamine group always remains significantly lower than the other 2 groups. The usual hypothermic effect of chlorpromazine, with a maximum intensity between 1 and 2 hours, is observed. Both pyribenzamine and dibenamine independently potentiate this hypothermic effect of chlorpromazine to an extent far greater than could be predicted from results obtained with these drugs alone. When dibenamine and pyribenzamine are added to chlorpromazine simultaneously, the intensity of the response is smaller and the recovery faster than could be anticipated on the basis of additive action.

Discussion. The possibility that chlorpromazine induces hypothermia by release of substances such as 5 hydroxytryptamine, some neurohumoral agent or histamine(5,6, 7,8), suggested that antagonists to the released substances might alleviate hypothermic effects of chlorpromazine. Experimental evidence, however, indicates that dibenamine and pyribenzamine potentiate rather than antagonize chlorpromazine. Evidence of potentiation between histamine and an antihistaminic with respect to gastric secretion has been given(10,11,12). It has been suggested that such an effect may be obtained if the antagonist competes with the active substance in some specific tissue(13). This hypothesis would suggest that antihistaminics increase blood levels of histamine and thus alter temperature regulating centers. The same may be true of dibenamine with regard to adrenaline, with the result that the level of adrenaline or some neurohumoral agent in circulation is increased. This increase would then result in a decreased oxygen consumption since adrenaline, while it increases the heat production at 94°F, will actually decrease the metabolic exchanges when injected into an animal kept at 72°F(8).

Summary. The hypothermic effect of dibenamine and pyribenzamine was observed

but was found to be of small intensity and short duration compared to that of chlorpromazine. Individually these drugs were found to potentiate the hypothermic effect of chlorpromazine to an extent far greater than could be predicted. Indeed, whereas dibenamine or pyribenzamine caused a drop in rectal temperature of less than 1°C, these drugs injected individually with chlorpromazine potentiated the effect of chlorpromazine on body temperature by 3 to 4°C. However, dibenamine and pyribenzamine antagonize one another when given simultaneously to animals treated with chlorpromazine; this antagonism further illustrates the complexity of action of these drugs.

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Synergism of Amines and Antagonism of Reserpine to Morphine Analgesia. (23656)

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It has been demonstrated(1) that reserpine antagonizes the analgetic effect of morphine in mice. Since reserpine is known to deplete tissues of 5-hydroxytryptamine(2) and catecholamines(3), experiments were performed to determine whether morphine analgesia was influenced by administration of various indolalkylamines and catecholamines and some of their derivatives.

Methods. Seven hundred sixty (760) white mice (Webster strain) with an average weight of 20 g were used. The tail of each mouse was subjected to a painful heat stimulus according to the technic of Gross(4) and the reaction time for the occurrence of the tail flick measured. The method has been previously described(1). The effects of morphine sulfate were studied alone and combined with reserpine phosphate, isoreserpine, 5-hydroxytryptamine, 5-hydroxytryptophane, 5-hydroxyindoleacetic acid, tryptophane, tryptamine, epinephrine, amphetamine, mescaline, iproniazid and choline-p-tolyl-ether. In addition, the influence of reserpine was observed on codeine and meperidine analgesia. All drugs were injected subcutaneously and dissolved in distilled water with the exception of isoreserpine which was dissolved in N, N-dimethylacetamide. The significance of the results was evaluated according to the ranking method described by Moroney(5)*.

Results. Table I illustrates and confirms the previous finding that reserpine antagonizes the morphine-induced prolongation of the reaction time in the tail flick test when

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