reduced by trypsin or heat, some of the inhibitory components appear to be proteins.

Failure of heparin to reduce inhibitory activities of tissue extracts furthermore suggests that inhibition is not the result of simple deactivation of clearing factor as a consequence of complex formation with polycations. Thus, *in vitro* inhibition of tissue clearing factor by Protamine which, as reported by Korn (8). is reversible by *in vitro* addition of heparin, differs from inhibition exerted by extracts described here.

Summary. Extracts of human rabbit tissues inhibited heparin-induced lipemia clearing activity of serum. Extracts of spleen, kidney and liver were strongly inhibitory; those of other organs exercised slight or moderate inhibition. The tissues contained inhibitory components which appear to be associated with proteins since they are nondialyzable. heat-labile and inactivated by trypsin.

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Bioassay of Ataractics Against Lethal Action of Mescaline in Mice. (24143)

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Current interest in mescaline has stimulated a search for agents with antagonistic actions. Thus, Deegan and Cook(1) have reported the protective effects of various centrally active agents against pruritic episodes induced by mescaline in mice. Spech(2) reported that mescaline induced bradycardia and hypoglycemia in rats, which could be reduced with fasting and epinephrine. The same author reported that mortality was unaffected by the use of barbiturates, curare, decamethonium or physostigmine.

It is the purpose of this study to demonstrate the protective effects of various ataractic agents against mescaline-induced mortality in mice.

Methods. Toxicity of mescaline in female CF_1 mice (18-22 g) was determined using the intravenous route. The LD_{95} was found to be 150 mg/kg in 610 animals. The typical response consisted of a very brief clonic seizure terminated by respiratory arrest in a matter of 2 to 3 minutes. The agents under study were administered intraperitoneally one hour prior to treatment with mescaline, with the exception of the following: meprobamate (20 min), benactyzine (5 min), diphenylhydantoin (40 min), reserpine (24 hours), trimethadione (40 min), serotonin (30 min), morphine (30 min), and amphetamine (30 min). Only base weight of the drug was used in determining dosage. Ten mice were used per dose level and at least 3 doses per drug were examined. In this study the end point of measurement was the survival or death of the animal 24 hours following mescaline injection. The per cent protection was plotted on log-probit paper and the effective dose 50%, the slope, and the fiducial limits were calculated according to the methods of Litchfield and Wilcoxon(3).

Results. In Table I are shown the PD_{50}'s (protective dose 50%) and slopes of the protective agents with their respective fiducial

TABLE I. Protective Effects of Ataractics against Mortality Induced by Mescaline in Mice.

	PD_{50}	Fiducial limits	S	Fiducial limits
*Chlorpromazine	4.5	2.5– 8.1	4.6	1.8–12
Perphenazine	4.5	3.1– 6.8	1.48	1.2– 2.0
Proclorperazine	10.0	7.3–13.5	1.7	1.4– 2.0
Thiopropazate	3.4	2.5– 4.6	1.5	1.2– 2.8
*Promazine	10.0	7.4–13.5	1.95	1.2– 3.1
Promethazine	15.0	13.1–17.1	1.3	1.1– 1.4
*Reserpine	2.5	1.4– 4.5	3.15	1.1– 8.8

* PD_{50} values only estimates since maximal protection exerted was 60 to 70%.

limits. As indicated, the most effective agents were thiopropazate, perphenazine, proclorperazine and promethazine with the following PD_{50}'s: 3.4, 4.5, 10.0 and 15.0 mg/kg. All 4 compounds brought about complete protection. On the other hand, reserpine, chlorpromazine and promazine did not exert complete protection and their PD_{50} values are only estimates since the maximal amount of protection was 60 to 70%.

No significant protection was obtained with the use of the following compounds at the dose ranges listed: sodium phenobarbital (3-96 mg/kg); meprobamate (10-160 mg/kg); benactyzine (3-40 mg/kg); atropine (1.5-48 mg/kg); hydroxyzine (Atarax)-(10-40 mg/kg); ethoxybutamoxane (3-96 mg/kg); SY-21 (N-ethyl-N-(9-fluorenyl)-2-aminoethylchloride HCl)-(1.5-16.0 mg/kg); diphenylhydantoin (5-20 mg/kg); trimethadione (1000-1500 mg/kg); LSD (Lysergic acid diethylamide) (1-4 mg/kg); serotonin (5-20 mg/kg); amphetamine (1-4 mg/kg); morphine (5-20 mg/kg); pyrilamine (Neo-antergan)-(3-48 mg/kg); diphenhydramine (Benadryl)-(6-24 mg/kg); iproniazid (Marsilid)-(10-800 mg/kg); pilocarpine (5-80 mg/kg); arecoline (5-80 mg/kg).

Discussion. The positive protective effects of chlorpromazine, perphenazine, proclorperazine, thiopropazate, promazine and reserpine against mescaline-induced mortality in mice have been demonstrated. The mechanism of action of these agents is probably central in nature for it is well known that they are characterized by a unique type of sedation. However, it has been reported that they also exert adrenergic blocking, anticholinergic, and antihistaminic properties(4,5). It was considered of interest to explore the possibility that one of these peripheral effects was active in protecting the animals. Agents classified as antihistaminics, anticholinergics, and adrenergic blocking agents, were examined for activity. Thus, peripheral adrenergic blockade produced by the specific adrenergic blocking agent, (N-ethyl-N-(9-fluorenyl)-2-aminoethylchloride hydrochloride)(6) and ethoxybutamoxane(7) did not prevent the toxic effects of mescaline. The anticholinergics, atropine and benactyzine, and the antihistaminics, pyrilamine and diphenhydramine, did not inhibit mortality. Finally, the sedatives and anticonvulsant, sodium phenobarbital, meprobamate and diphenylhydantoin, were found to exert no protection. In addition, stimulants and analgesics, represented in this study by amphetamine and morphine, were ineffective.

Since the antihistaminic, adrenergic blocking and anticholinergic agents were ineffective against the lethal effects of mescaline, it is highly probable that the protective effects of the ataractics are exerted centrally. Thus, Marrazzi and Hart(8,9) have reported that chlorpromazine and reserpine block the effects of mescaline in a 2-neuron intercortical (trans-

TABLE II. Inactive Agents against Mortality Induced by Mescaline in Mice.

Agent	Pretreatment time	Doses tested, mg/kg, I.P.
Sodium phenobarbital	1 hr	3, 6, 12, 24, 48, 72, 96
Meprobamate	20 min.	10, 20, 40, 80, 160
Benactyzine	5 "	3, 6, 10, 12, 20, 40
Atropine	1 hr	1.5, 3, 6, 12, 24, 48, 100
Hydroxyzine	1 "	10, 20, 40
Ethoxybutamoxane	1 "	3, 6, 12, 24, 48, 96
SY-21	1 "	1, 2, 4, 8, 16
Diphenylhydantoin	40 min.	5, 10, 20
Trimethadione	40 "	1000, 1250, 1500
Lysergic acid diethylamide	1 hr	1, 2, 4
Serotonin	30 min.	5, 10, 20
Amphetamine	30 "	1, 2, 4
Morphine	30 "	5, 10, 20
Pyrilamine	1 hr	3, 6, 12, 24, 48
Diphenhydramine	1 "	6, 12, 24
Iproniazid	1 "	10, 20, 40, 50, 100, 200, 400, 800
Pilocarpine	1 "	5, 10, 20, 40, 80
Arecoline	1 "	*Idem*

callosal) system. It would be, indeed, an interesting problem in mechanism of action to study the interactions of these agents at the enzymatic level.

Summary. 1. It has been demonstrated that chlorpromazine, perphenazine, proclorperazine, promazine, thiopropazate, promethazine and reserpine are effective antagonists of mescaline-induced mortality in CF_1 mice. 2. No significant protection was found with use of sodium phenobarbital, meprobamate, benactyzine, atropine, hydroxyzine, ethoxybutamoxane, SY-21, diphenylhydantoin, trimethadione, lysergic acid diethylamide, serotonin, amphetamine, morphine, pyrilamine, diphenhydramine, iproniazid, pilocarpine, and arecoline. 3. It is suggested that the protective effects of the ataractics against mescaline-induced mortality are centrally mediated.

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Submicroscopic Morphology of Avian Neoplasms I. Studies on Erythroblastosis.* (24144)

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Electron microscope studies of ultrathin sections of cells infected with a number of different viruses have revealed the structure of various submicroscopic cell elements during different stages of infection and have showed the complicated structure of the viruses in cells and tissues. The observation that viruses can be detected in diseased tissues and that they can be differentiated from normal cell constituents has in turn led to electron microscope studies of tumors of known or suspected viral origin(1,2). The neoplastic conditions now classified in the chicken leukosis complex were the first tumors induced by filterable agents(3). Some tumors of the fowl leukosis complex, such as visceral lymphomatosis(4), osteopetrosis(4), erythroblastosis and myeloblastosis (granuloblastosis)(5) have been transmitted by cell-free preparations. Other conditions, such as neuro-lymphomatosis and ocular lymphomatosis, have not as yet been transmitted by cell-free preparations. Extensive studies have been carried out to ascertain the physical, chemical, immunologic and other properties of the viral agents present in cell-free preparations(5). Electron microscope studies on the morphology of particulate material in cell-free preparations, which had been dehydrated and shadowed, were also carried out to characterize agents responsible for erythroblastosis, myeloblastosis and lymphomatosis(5). Recently, the technic of ultrathin sectioning has been applied to ultracentrifugal pellets from plasmas of chickens with myeloblastosis and erythroblastosis(6). These studies revealed the characteristic structure of particles present in the ultracentrifugal

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