indicated by the infectivity of the various suspensions shown in Table II. The effluent from the resin-tissue-virus complex is non-infective indicating that the virus is retained with the resin. Before attempting to elute the virus from the resin, the complex was thoroughly washed with distilled water to remove any tissue fragments which might contain virus. The wash fluid was occasionally infective (Table I). Aliquots of the resin-tissue-virus complex were then treated with solutions containing different salts at high concentration and at varying pH. Five and 10% solutions of sodium chloride and sodium bicarbonate, and a 5% solution of disodium acid phosphate did not elute the virus from the resin. However, the virus was eluted with a 10% solution of disodium acid phosphate. It appears that the virus is almost selectively eluted with a high concentration of disodium acid phosphate, leaving the bulk of the nitrogenous material adsorbed to the resin (Table I).

Similar results were obtained in the extraction of poliomyelitis virus from pooled human stools of known infectivity. The final eluate which was clear and colorless contained 9.2 γ of total nitrogen as compared with 236 γ of total nitrogen in the starting suspension. The infectivity of the material was retained as shown by the development of paralysis in 1 of 2 monkeys 7 days after intracerebral injection of 1 ml of the final eluate.

Comment. Muller(14) has recently reported the use of a *cation* exchange resin for partial purification of such neurotropic viruses as the Japanese B encephalitis, Eastern equine encephalomyelitis and Western equine encephalomyelitis. The mode of action of Muller's cation exchange resin in effecting a partial purification of virus differs from that of the anion exchange resin reported in this paper. With the use of the *cation* exchange resin, extraneous nitrogenous material is adsorbed to the resin, leaving the virus in the effluent. On the other hand, with the use of the *anion* exchange resin, it is possible to adsorb viruses to the resin along with the nitrogenous material. The virus is then selectively eluted from the resin.

Summary. A simple and rapid procedure for the partial purification of certain viruses is afforded by the use of a strong-base anion exchange resin (Amberlite XE-67). A clear, colorless solution is obtained which retains its original infectivity but which has lost at least 90% of its nitrogenous material.

14. Muller, H. R., PROC. SOC. EXP. BIOL. AND MED., 1950, v73, 239.

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Anticonvulsant Action of Isopropyl Alcohol.* (17857)

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In previous reports from this department (1,2), it has been shown that isopropyl alcohol can significantly increase the blood acetone and the cortical threshold to electrical stimulation in different species. Since the maximum acetonemia after gastric administration of the isopropyl alcohol did not strictly coincide with the peak of cortical threshold, further examination of the possible mechanism of the anticonvulsant action has been made.

Methods. The cortical threshold was de-

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1. Driver, R. L., PROC. SOC. EXP. BIOL. AND MED., 1947, v64, 248.

2. Chu, N., Driver, R. L., and Hanzlik, P. J., *J. Pharm. Exp. Therap.*, 1948, v92, 291.

termined according to the method described by Tainter and associates(3). With increasing amperage, current was passed through the brain for 2.0 seconds at 5-minute intervals until a tonic-clonic convulsive seizure was elicited. Blood acetone was determined by the micromethod of Greenberg and Lester (4). Blood isopropyl alcohol was estimated by a modification of the vacuum distillation, iodometric procedure for ethyl alcohol described by Newman(5).

Gastric administration of isopropyl alcohol. Twenty-two rats and 6 rabbits were each given gastrically the optimal single dose of isopropyl alcohol (1250 mg/kg). Higher doses produce ataxia. Determinations of blood alcohol and acetone and cortical threshold were made 1 hour before and at intervals of 0.5, 1, 3, and 6 hours after the medication. The average results are presented in Fig. 1 and 2. Throughout the period of observation, the cortical threshold in both species rose and fell in a curve approximately parallel to the curve for the blood isopropyl alcohol; while the blood acetone had not reached a peak long after the maximum cortical depression had been achieved.

Repeated gastric administration of isopropyl alcohol. Three rabbits were each given 1250 mg/kg gastrically, in equally divided doses, 3 times daily for 3 days. Determinations of cortical threshold and blood acetone were made every morning before, and 1 hour after, each dose. The results are presented in Fig. 3 with the course of cortical thresholds in 3 unmedicated rabbits. Despite a cumulative increase in blood acetone, the daily peaks in cortical threshold showed a diminishing magnitude and each day returned nearly to a zero value. These results confirmed a lack of correlation between cortical depression and blood concentration of acetone.

Intravenous injections of acetone and of isopropyl alcohol. In an attempt to quantitate the share contributed by the acetone and the alcohol in elevating the cortical threshold, these agents were injected intravenously in different groups of rats to produce graded blood levels. Determinations of the cortical thresholds were made 1 hour before, and im-

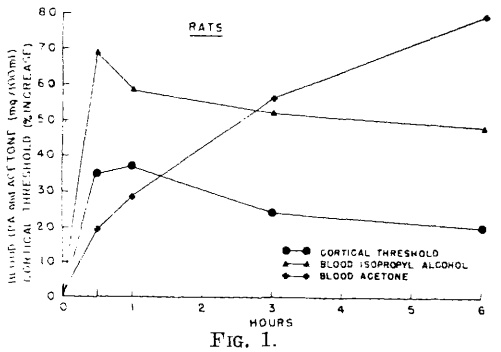

FIG. 1.

Cortical threshold, blood alcohol, and blood acetone following a single gastric dose of isopropyl alcohol, 1250 mg/kg. Averages of 22 rats.

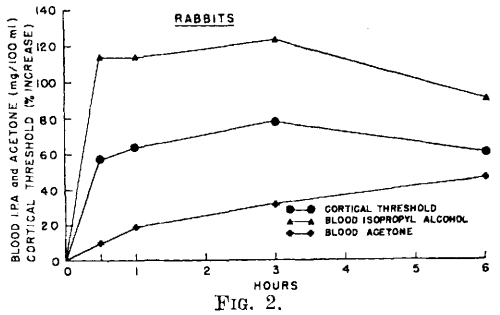

FIG. 2.

Cortical threshold, blood alcohol, and blood acetone following a single gastric dose of isopropyl alcohol, 1250 mg/kg. Averages of 6 rabbits.

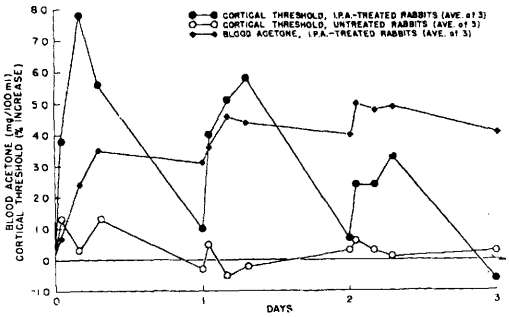

FIG. 3.

Cortical threshold and blood acetone of rabbits which were given isopropyl alcohol gastrically, 1250 mg/kg in 3 equally divided doses daily.

3. Tainter, M. L., Tainter, E. G., Lawrence, W. S., Neuru, E. N., Lackey, R. W., Luduena, F. P., Kirtland, H. B., and Gonzales, R. I., *J. Pharm. Exp. Therap.*, 1943, v79, 42.

4. Greenberg, L. A., and Lester, D., *J. Biol. Chem.*, 1944, v154, 177.

5. Newman, H., *J. Pharm. Exp. Therap.*, 1936, v56, 278.

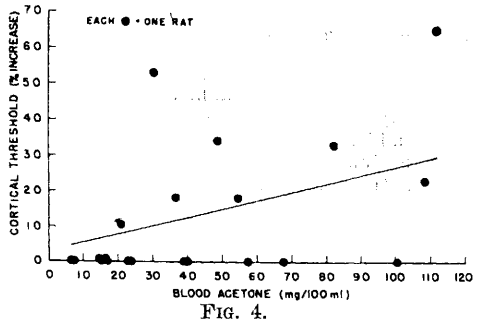

FIG. 4.

Intravenous administration of acetone in rats. ($Y = a + bX$).

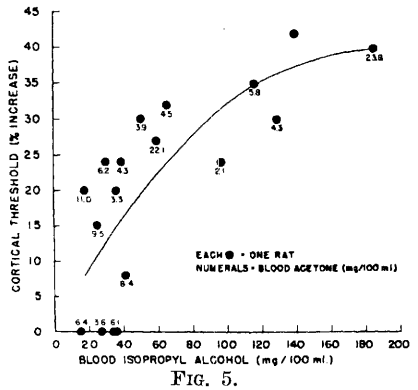

FIG. 5.

Intravenous administration of isopropyl alcohol in rats. ($Y = a + bX + cX^2$).

mediately after, injection. The per cent increase in threshold was plotted against the blood levels of acetone and of isopropyl alcohol (Fig. 4 and 5).

Fig. 4 shows there was a great scatter of values after the intravenous acetone. When the blood acetone was less than 30 mg/100 ml, there was no significant increase in the cortical threshold. Changes of 10% were within the range of experimental error. Over the range of 30 to 110 mg of acetone/100 ml, half of the rats convulsed at the control threshold value, and half had variable threshold increases (18 to 65%). Thus, even at extremely high concentrations of blood acetone, there was no consistent depression of the cortex to electrical stimulation. When isopropyl alcohol was injected, there was less scatter of values (Fig. 5). With blood alcohol levels less than 20 mg/100 ml, there was no significant elevation of cortical threshold; between 20 and 40 mg/100 ml, 4 rats showed no increment in threshold, but 5 rats had elevations of 15 to 24%. In the range of 40 to 183 mg/100 ml, all thresholds were raised significantly (24 to 42%). As higher blood alcohol levels (*ca* 120 mg/100 ml) were reached, there was leveling of the curve, which suggested that the maximum depressant effect had been reached. Since blood samples were drawn within 60 seconds after injection, very little of the isopropyl alcohol had been oxidized to acetone; and the corresponding blood acetone concentrations were low, usually only 1 to 5 mg/100 ml above normal. On the basis of the observations with injected acetone, none of the acetone values in this experiment was great enough *per se* to reduce appreciably the susceptibility of the cortex to electrical stimulation.

Other alcohols. Since these experiments suggested that the anticonvulsant effect of isopropyl alcohol was produced by the alcohol itself, it was of interest to test other alcohols. The results with 4 different alcohols given gastrically to rats are summarized in Table I.

Ethyl alcohol, which yields acetaldehyde rather than acetone, elevated the cortical threshold only after very high doses (7.5 to 10.0 g/kg), which caused definite to marked motor depression. The secondary alcohols, 2-butanol and 3-pentanol, at lower optimum doses (0.5 to 0.75 g/kg, respectively) compared favorably with isopropyl alcohol in raising the cortical threshold but the highest dose caused marked ataxia. 3-Pentanol (0.5 and 0.75 g/kg) yielded comparatively minor increases in blood acetone. The tertiary alcohol, 2-methyl-2-butanol, 0.5 g/kg, produced marked cortical and motor depression without increase in blood acetone.

Chemical convulsants. Tests for isopropyl alcohol antagonism of chemically-induced convulsions were made against the following agents: metrazol, picrotoxin, and thujone (cedar leaf oil). For comparison, similar tests were made with the anticonvulsants, phenobarbital sodium and diphenylhydantoin sodium. For control, the convulsants were given in different doses to groups of 20 rats each. Metrazol, 10%, and picrotoxin, 0.3%, were administered subcutaneously. Oil of

TABLE I.
Various Alcohols on Cortical Threshold, Alcoholemia, Acetonemia and Motor Depression.

Alcohol	Gastric dose (g/kg)	No. of rats	Cortical threshold (% incr.) Avg	Cortical threshold (% incr.) Range	Avg incr. in blood acetone (mg/100 ml)	Avg incr. in blood alcohol (mg/100 ml) Avg	Avg incr. in blood alcohol (mg/100 ml) Range	Motor depression
				Primary				
Ethyl alcohol	2.5	5	0	0				0
	5.0	5	8	0– 38		74	34–132	0
	7.5	5	14	0– 55		100	80–108	Present
	8.5	5	52	0–130				Marked
	10.0	5	45	0– 81				,,
				Secondary				
2-butanol*	.5	5	46	33– 60	18	15	5– 27	0
	.75	8	40	23– 57	24	69	17– 96	0
	1.0	5	85	54–128	31			Marked
3-pentanol†	.5	5	28	8– 43	6			0
	.75	3	33	22– 82	5			Marked
				Tertiary				
2-methyl-2-butanol‡	.5	5	67	40–112	0			,,

* or secondary butyl alcohol.
† or diethyl carbinol.
‡ or tertiary amyl alcohol.

TABLE II.
Isopropyl Alcohol and Other Anticonvulsants Against Chemical Convulsants.
20 rats in each experiment.

Anticonvulsant*	Total convulsions No.†	P	Max. convulsions No.‡	P	Total convulsions No.†	P	Max. convulsions No.‡	P◊
				Metrazol.				
	35 mg/kg				50 mg/kg			
None	7		3		20		15	
Isopropyl Alcohol	0	.01	0	.32	15	.01	2	.0009
Diphenylhydantoin	5	.30	4	.39	17	.32	16	.39
Phenobarbital	0	.01	0	.32	8	.0005	7	.08
				Picrotoxin.				
	2 mg/kg				3 mg/kg			
None	19		16		20		20	
Isopropyl Alcohol	15	.39	6	.004	19	.39	17	.16
Diphenylhydantoin	7	.0005	6	.004	16	.12	16	.12
Phenobarbital	6	.0005	4	.0005	14	.02	10	.0005
				Thujone.				
	14 mg/kg				16 mg/kg			
None	10		10		19		17	
Isopropyl Alcohol	9	.39	3	.04	10	.004	4	.0005
Diphenylhydantoin	17	.04	17	.04	16	.32	15	.39
Phenobarbital	8	.39	7	.39	16	.32	8	.008

* The doses of the anticonvulsants throughout were as follows: isopropyl alcohol, 1250 mg/kg; diphenylhydantoin, 100 mg/kg; phenobarbital, 50 mg/kg.
† Number of rats showing min. and max. clonic seizures.
‡ Number of rats showing maximum convulsons.
◊ When P is less than 0.05 the difference is significant.

cedar leaf, containing 60% thujone, was given intraperitoneally as a 10% solution in 95% ethyl alcohol. The rats were observed for 1 hour. Convulsions were recorded both as to incidence and severity: brief but definite bursts of clonic twitching were included in the total convulsions; while generalized, prolonged, tonic-clonic seizures were maxi-

mal. Other groups of 20 rats each were gastrically premedicated with single doses of isopropyl alcohol, 1250 mg/kg, diphenylhydantoin, 100 mg/kg, or phenobarbital, 50 mg/kg; and 1 hour later these rats were given the convulsants in the same doses as in the controls. The doses of isopropyl alcohol and phenobarbital were those found previously to be the maximal which would not produce undesirable motor depression.

In doses which did not cause motor ataxia, isopropyl alcohol compared favorably with phenobarbital in preventing and ameliorating the convulsions of metrazol. This alcohol was superior to phenobarbital in antagonizing thujone seizures; but the alcohol was less effective than phenobarbital against picrotoxin. Diphenylhydantoin afforded protection against picrotoxin convulsions only.

Summary. Analyses of blood isopropyl alcohol and blood acetone in relation to elevation of cortical threshold to electric stimulation suggest that the alcohol itself is responsible for the anticonvulsant effect. The ketonemia, nonetheless, may contribute a share. Other secondary and tertiary alcohols (2-butanol, 3-pentanol, and 2-methyl-2-butanol) effectively raised the cortical threshold, with or without acetonemia. Isopropyl alcohol was capable of antagonizing metrazol and thujone convulsions but was not effective against picrotoxin seizures.

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Therapy of Paroxysmal Pulmonary Edema by Anti-Foaming Agents (17858)

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In spite of accepted therapeutic measures, paroxysmal pulmonary edema still has a high mortality. For this reason, any new drug or aid may be of importance. It has long been known(1) that large amounts of fluid may be tolerated in the respiratory passages as long as no foam is formed. When the latter occurs, increased volume of the fluid and modified physical properties cause severe effects by blocking the small bronchi and adding the effects of anoxia to those already causing pulmonary edema. For this reason, a systematic study of several anti-foaming agents introduced into the respiratory passages was undertaken.

Material and method. The study was made in a series of 100 white, male rabbits weighing between 1.6 and 2 kg. Paroxysmal pulmonary edema was induced by the standard method previously used by the author(2) and slightly modified by Glass(3). Adrenalin Parke and Davis was injected slowly into the marginal vein of the ear, 2 cc of the one to one thousand solution being injected in one minute. The following anti-foaming substances were tested: (a) ether; (b) octyl alcohol;† (c) capryl alcohol;‡ (d) 95% ethyl alcohol; (e) sorbitan triolate (Span 85).§ The rabbits were placed into a box with a glass cover and each of the above drugs was sprayed into it at frequent intervals by means of an atomizer. The action of the drug was prolonged for 10 minutes prior to the injection of adrenalin and then until

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2. Luisada, A. A., *Arch. Exp. Path. u. Pharm.*, 1928, v132, 313.

3. Glass, A., *Arch. Exp. Path. u Pharm.*, 1928, v136, 72.

† n-octyl alcohol, supplied by Eastman Kodak Co.

‡ methyl-n-hexacarbinol, supplied by Eastman Kodak Co.

§ This substance was obtained through the courtesy of the Atlas Powder Co.