For instance, Frank, Seligman, and Fine(3) described a similar syndrome in dogs which had been subjected to exsanguination to shock levels, and then reinfused with blood, which had been collected in non-sterile containers, in an effort to evaluate the stage of irreversibility of shock. The similarity of this syndrome to that seen on occasion in human patients is striking(4).

Waisbren has found that patients with advanced cirrhosis not infrequently develop a hemorrhagic syndrome in association with Gram-negative spore-former bacteremia(5).

Aub and his associates reported that many of the effects of trauma to muscle in the dog are attributable to contaminating Clostridia and concluded with a plea for care in eliminating sepsis in muscle trauma experiments(6). Our present report extends the scope of the importance of asepsis and calls attention to the lethal effect of organisms previously considered non-pathogens.

Conclusion. Dogs receiving an intravenous infusion of a 14 hour culture of the Paracolon Bacillus exhibited profound illness and rapid death. Canine experiments in which conclusions are to be based on survival in apparent health for more than 2 or 3 hours should be conducted with precise aseptic technic rather than general cleanliness alone, in order to eliminate the influences of bacterial contamination.

The authors express thanks to Dr. J. T. Syverton for kindly counsel and aid in the prosecution of this study.

3. Frank, H. A., Seligman, A. M., and Fine, J., *J. Clin. Invest.*, 1945, v24, 435.

4. Friesen, S. R., and Nelson, R. M., *Southern Surgeon*, 1951, in press.

5. Waisbren, Burton A., personal communication.

6. Aub, J. C., Brues, A. M., Dubos, R., Kety, S. S., Nathanson, I. T., Pope, A., and Zamecnik, P. C., *War Med.*, 1944, v5, 71.

Received February 28, 1951. P.S.E.B.M., 1951, v76.

Central Nervous System Activity of Some 2-Pyridyl Compounds.* (18614)

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In studies employing our previously described technics used in screening drugs for anti-convulsant activity(1), a variety of chemical structures containing a 2-substituted pyridine grouping have been investigated (Table I). Several piperidine and quinoline compounds of similar configuration have been examined for comparative purposes. The syntheses of a large majority of these compounds have been described recently by Boekelheide and Agnello(2).† The pharmacological actions of previously studied pyridine derivatives have been reviewed by Von Oettinger(3). More recently Fromherz and Spiegelberg(4,5) have investigated a series of 3-substituted pyridine compounds from a pharmacodynamic viewpoint, and Valenzuela and Huidobro(6) have studied the effects of some similar compounds upon neuromuscular transmission. No studies of the presently considered 2-substituted pyridine compounds re-

* Aided by a grant from the National Foundation for Infantile Paralysis.

1. Slater, I. H., O'Leary, J. F., Leary, D. E., *J. Pharmacol.*, 1950, v100, 316.

2. Boekelheide, V. and Agnello, A. J., *J. Am. Chem. Soc.*, 1950, v72, 5005.

† These investigators have kindly supplied us with these compounds.

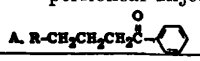
3. Von Oettingen, W. F., *The Therapeutic Agents of the Pyrrole and Pyridine Groups*, Edwards Brothers, Inc., Publishers, Ann Arbor, Mich., 1936.

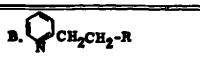
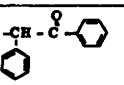
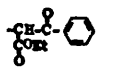
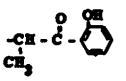
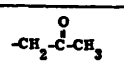
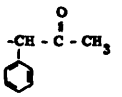
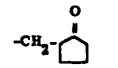
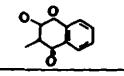
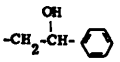
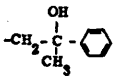
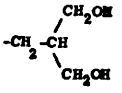
4. Fromherz, K., *Schweiz. Med. Wochensch.*, 1949, v79, 521.

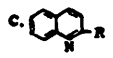
5. Fromherz, K., Spiegelberg, H., *Helv. Physiol. Acta*, 1948, v6, 42.

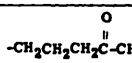
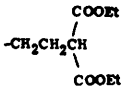
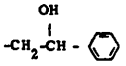
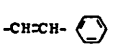
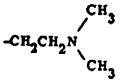
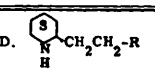
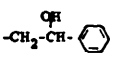
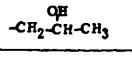
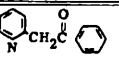
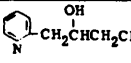
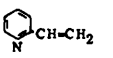
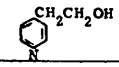
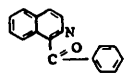
6. Valenzuela, F., and Huidobro, F., *J. Pharmacol.*, 1948, v92, 1.

TABLE I. Mean Paralyzing, Anticonvulsant, and Lethal Doses of Some Pyridyl, Piperidyl, and Quinolyl Compounds After Intraperitoneal Injection in White Mice.

A. 

Code	R, Substituent	LD_{50}	ED_{50}	PD_{e50}	$\frac{LD_{50}}{ED_{50}}$	$\frac{LD_{50}}{PD_{e50}}$
		mM/kgm	mM/kgm	mM/kgm		
EJA K		0.89 ±.06	0.27±.02	.034±.014	3.3	10.7
M-3167		1.37 ±.12	0.68±.05	0.22 ±.03	2.0	6.2
VB-25		.085±.012	None	None	-	-
170-2		0.64 ±.11	Convulse	0.21±.02	-	3.2
	B. 					
M-66		1.27 ±.19	Convulse	0.48*	-	2.6
M-66-2		2.6	2.14±.31	0.44±.17	1.2	5.9
EJA V		3.2 ±.18	1.9 ±.29	0.47	1.7	6.8
VB-19		1.7	1.4	None	1.2	-
M-16-1		1.88 ±.21	0.55±.01	0.26±.15	3.4	7.2
M-5		1.8	1.5	None	1.2	-
EJA III		0.15 ±.03	None	None	-	-
M-11		1.88 ±.07	0.59 ±.03	0.24±.01	3.2	7.8
M-3066		2.31 ±.18	0.85±.09	0.25±.19	2.7	9.2
VB-15		4.8	None	None	-	-
VB-10	$-CH_2OH$	6.6	None	None	-	-
VB-11	$-OH$	11.4	None	None	-	-

C. 

Code	R, Substituent	LD_{50}	ED_{50}	PD_{e50}	$\frac{LD_{50}}{ED_{50}}$	$\frac{LD_{50}}{PD_{e50}}$
179-1		2.30 ±.12	1.45±.09	0.71	1.6	3.6
M-105		1.81 ±.30	None	None	-	-
M-86		3.1	Partial	0.46±.07	-	6.7
M-86-1		2.7	None	None	-	-
M-2-D	$-CH_2CH_2OH$	4.0	2.0	1.3	2.0	3.1
M-52-3		0.75 ±.05	None	None	-	-
	D. 					
M-3678		0.38 ±.03	None	None	-	-
VB-16		0.89 ±.13	None	None	-	-
VB-12	$-CH_2OH$	1.5	None	None	-	-
	E. Other Compounds					
AEA-3		2.2 ±.19	1.5 ±.12	0.47±.06	1.2	4.7
WG-13-6		4.1 ±.63	3.2 ±.50	1.2 ±.10	0.8	2.9
VB-18		2.7	None	None	-	-
VB-14		10.8	None	None	-	-
W-48-1		1.05	None	None	-	-

* Values showing no standard errors were obtained from data having no intermediate partial responses between total response and no response, due to the extreme steepness of the regression lines of these assays. Inclusion of extra intermediate dose level groups was precluded in most cases by lack of adequate amounts of the compounds. The error of these values should not exceed ± 25%.

lating to central nervous action have been described.

Experimental. Table I shows the dose of the various compounds administered to mice required to paralyze half the animals (ED_{50}, loss of righting reflex). Also shown are the doses required to protect half the mice against the tonic phase of maximal electrical seizure pattern induced by a shock of 8 milliamperes of current applied for 0.5 second through ear electrodes. The ratios of these doses to the median lethal dose are given also for each compound. In most instances, several groups of 5 or 10 mice each were used to determine each value shown. The various dosages shown in Table I were obtained together with their standard errors where shown, by the plotting procedure of Miller and Tainter(7).

These compounds showed no significant protection against strychnine or metrazol convulsions in experiments in which 2 lethal doses of the convulsant were injected into mice intraperitoneally 5 minutes after the intraperitoneal administration of the compound to be tested. Survivals at the end of one hour were counted and a mean protecting dose, if any, was calculated.

EJA II, phenyl γ-(2-pyridyl) propyl ketone, was the most potent compound studied.

Discussion. It is noteworthy that many of these compounds exhibit potent action both as paralyzing agents and as anti-convulsants against electro-shock. However, the great majority of these compounds were characterized by a short duration of action, *viz.*, 5 to 20 minutes. Since our screening procedures measure protective activity against strychnine or metrazol for one hour, few of the compounds appeared to be effective anti-convulsants against these agents although in many cases there was a significant prolongation of survival time. Protection technics utilizing intravenous titration-to-convulsion or death(8) measure the instantaneous potency of the anticonvulsant without the immediate consideration of the probable duration of action. Such studies should provide more useful information concerning the site of action of anti-convulsant drugs having short action. These compounds have been found to be primarily central nervous depressants, although in two instances (M-85 and 170-2) stimulant activity is observed as indicated by excitement and convulsions (Table I). In mice the depressant action is characterized in most cases by an initial arching of the neck and stiffening of the limbs, with paralysis ensuing shortly thereafter. A similar action has been observed in preliminary experiments on rats, rabbits, and cats.

Because of the short duration of action of these compounds, they show little promise of clinical application at present. However, in view of their interesting central action, further studies on these and related compounds are being undertaken.

7. Miller, L. C., and Tainter, M. L., PROC. SOC. EXP. BIOL. AND MED., 1944, v57, 261.

8. Orloff, M. J., Williams, H. L., and Pfeiffer, C. C., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 254.

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Distribution of Radioactivity in the Egg after Feeding Sodium Acetate-1-C^{14}* (18615)

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Earlier work on the distribution of radioactivity in eggs following the administration of radioactive isotopes of phosphorus, strontium and iron has been discussed in the com-

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