instillations of virus one day and again 18 days later. Three additional monkeys so treated resisted virus instillations 2, 31 and 57 days later. Further instillations to determine the duration of the resistance remain to be made.

In all of the virus instillations referred to above the controls generally equalled the animals treated with a given reagent and the percentage of infection in the parallel control group averaged above 90%. The intranasal irrigations with the chemical solutions indicated were all carried out thoroughly while the animals were under ether anesthesia and held in a special vertical holder, with the head downward.

Further studies are in progress not only with the reagents above mentioned, but with a number of others, including a variety of dye stuffs, chosen particularly for their potential ability to modify the permeability of the normal portal of entrance of this virus. Among the various possibly effective agents may be one or more which may prove effective, agreeable, and harmless enough for prophylactic application in man during epidemic periods.

8530 C

Acute Toxicities of Rotenone and Mixed Pyrethrins in Mammals.

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Rotenone and pyrethrum are proposed as harmless substitutes for inorganic insecticides,[1] and mixed pyrethrins are recommended as anthelmintics[2] and as scabicides.[3] The only critical report on the toxicity of rotenone in mammals is by Haag,[4] who indicates that there is little if any danger of acute intoxication following the ingestion of foodstuffs sprayed with rotenone. Chevalier[2] states that pyrethrum orally produces no untoward effects even when given to children.

In order to ascertain the probable toxic range of rotenone* or

[1] Roark, R. C., *Ind. Eng. Chem.*, 1935, **27**, 530.

[2] Chevalier, J., *Bull. l'acad. de Med.*, 1928, **99**, 446.

[3] Sweitzer, S. E., and Tedder, J. W., *Minn. Med.*, 1935, **18**, 793.

[4] Haag, H. B., *J. Pharmacol. Exp. Therap.*, 1931, **43**, 193.

* Kindly supplied by Dr. R. C. Roark, Insecticide Division, Department of Agriculture, Washington, D. C.

mixed pyrethrins† after absorption into the body, these drugs were given intraperitoneally or orally to guinea pigs, rats, and mice in 0.1-14% dilutions in ethylene glycol or petroleum oil, respectively, Animals were observed for one month. Controls, given the solvents alone, were unaffected over the period of observation.

1. Rotenone injected intraperitoneally killed half or more of the animals in doses of 2 to 10 mg. per kg. (Table I). Death occurred within 30 minutes in 50% of the fatalities, and within 14 days in the remainder. Toxic symptoms noted were: respiratory depression, incoordination, clonic convulsions, muscle tremors, and death due to respiratory failure. At necropsy one-third of the dead animals showed pulmonary congestion; no peritonitis or ulceration at the site of the injection were encountered.

Orally, the drug was given in powder form in gelatine capsules to guinea pigs, and in a 1% dilution in ethylene glycol by rubber tube to lightly anesthetized rats. The average minimal killing dose was 75 to 100 mg. per kg., and, as on intraperitoneal injection, was more toxic for rats than for guinea pigs (Table I). Thirty per cent of the fatalities occurred in 4 to 24 hours, 50% in 24 to 48 hours, and the rest in 3 to 10 days. Seventy per cent of the dead animals showed pulmonary congestion of varying degrees, and in 40% the mucosa of the stomach was reddened or sloughed. The animals surviving lost up to 10% of their initial weight in 3 days, but gradually regained it.

One per cent rotenone placed into a rabbit's eye produced immediate irritation and a transitory reddening of the conjunctiva. The solvent caused no effect.

TABLE I.
Acute Toxicity of Rotenone, in Ethylene Glycol.

	Dose in mg./kg.	Ratio of deaths to number of animals used		
		Mice	Rats	Guinea Pigs
Intraperitoneal:				
	1		0/9	
	2	0/10	11/14	0/5
	3		4/5	
	5	8/10	10/10	0/10
	10	9/10		5/15
	15			9/10
	20			4/5
Oral:				
	50		2/10	
	75		6/10	0/8
	100		8/10	4/10
	200		10/10	8/10

† Kindly supplied by Dr. C. B. Gnadinger, McLaughlin-Gormley-King Co., Minneapolis, Minnesota.

Investigation of the chronic toxicity of rotenone given orally has shown that only one of 8 guinea pigs died after receiving 4 doses of 25 mg. per kg. in 10 days.

2. The mixed pyrethrins were used in 0.1 to 2.4% dilutions in petroleum oil, or as the oleoresin, containing 14% of pyrethrins I and II according to Gnadinger.[5] Injected intraperitoneally, the mixed pyrethrins killed at 100 to 150 mg. per kg. (Table II). The symptoms of toxicity noted were: increased respiratory rate, hyperexcitability, incoordination, tremors and paralysis, and death due to respiratory failure. Hyperexcitability at times continued for over 24 hours. One-third of the animals dying succumbed in 10 to 24 hours, one-third in 3 to 5 days, and the rest within 22 days. A small number of animals died almost immediately after injection of small amounts of the substance. Sixty per cent of the necropsied animals showed pulmonary congestion, and 10% had adhesive peritonitis.

TABLE II.
Acute Toxicity of Mixed Pyrethrins, in Petroleum Oil.

	Dose in mg./kg.	Ratio of deaths to number of animals used		
		Mice	Rats	Guinea Pigs
Intraperitoneal:				
	25	2/10		
	50	3/10	1/10	2/10
	100	5/10	3/10	5/10
	150	6/10	9/15	6/10
	200	10/10	13/15	9/10
Oral:				
	500		0/10	
	1000		0/9	1/10
	1500		0/6	5/8

The oral doses were administered by rubber tube, to lightly anesthetized animals. One-half of the guinea pigs died at 1500 mg. per kg., while rats tolerated this dose. Larger amounts could not be given safely, *i. e.*, without rupturing the stomach. The guinea pigs died in 48 hours, and at necropsy two-thirds (including some killed later) had pulmonary congestion, about half had damaged gastric mucosa, and one showed peritonitis. The survivors lost 10-15% of their initial weight and appeared ill for several days. The drug solution caused a yellow discoloration in the anal region in 2 to 3 hours, in several, and diarrhea, lasting 24 hours, was present in half of the animals. Rats given large amounts of mixed pyrethrins

[5] Gnadinger, C. B., Pyrethrum Flowers, McLaughlin-Gormley King Co., Minnesota, 1933.

showed hair loss and skin irritation around the anal region; this occurred less frequently in the guinea pigs.

Mixed pyrethrins, 2.4% rubbed into the hair and skin of six animals, produced no hair loss or skin irritation in rats or guinea pigs. One per cent pyrethrum placed into a rabbit's eye produced no immediate irritation, but a conjunctival bleb formed in 6 hours.

Mixed pyrethrins given in single doses of 500 mg. per kg. and repeated 6 times in 2 weeks (total administration of 3.0 gm. per kg.) killed 2 out of 8 rats.

8531 C

Acute Intraperitoneal Toxicity of Some Plant Growth Substances for Mice.

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Zimmerman and Wilcoxon[1] report the rooting and bending responses of plants to various "growth-promoting" compounds. Of the agents we studied, they find the per cent concentrations necessary for positive bending or injury to be (in order of decreasing toxicity): indolacetic acid 0.5; alpha-naphthalenacetic acid 1.5; indolproprionic acid 2.0; indolbutyric acid 2.0; and phenylacetic acid 3.0. In the human body the indole acids are derived presumably from tryptophane, and indolacetic acid can be recovered from urine. In carcinomata indolacetic acid occurs in concentration twice that of surrounding tissues according to Kögl, Haagen-Smit and Tönnis.[2]

We desired to determine whether any correlation exists between the relative toxicity of these compounds for plants and their relative toxicity in mammals. Mice, observed for 4 weeks, were used as test animals. The substances were dissolved in water or di-ethylene glycol, and fresh 1% dilutions were injected intraperitoneally. Indolacetic acid* kills half or more of the animals injected at 25 mg. per kg., alpha-naphthalenacetic acid† at 100 mg. per kg., indol-

[1] Zimmerman, P. W., and Wilcoxon, F., *Contrib. Boyce Thompson Institute*, 1935, **7**, 209.

[2] Kögl, F., Haagen-Smit, A. J., and Tönnis, B., *Z. Physiol. Chem.*, 1933, **220**, 162; Kögl, F., Haagen-Smit, A. J., and Erxleben, H., *Z. Physiol. Chem.*, 1933, **220**, 137.