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Acute Toxicity for Mice of Phthalic Acid and Certain Derivatives.*

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Although a number of reports have appeared describing the toxic properties of diethyl phthalate,[1-5] a single report is available on dimethyl phthalate[6] and none on phthalic acid, sodium phthalate, dibutyl phthalate or dioctanol 2 phthalate.

Acute Toxicity for Mice. Intraperitoneal injections of the various compounds were given to 3-months-old, male, white mice. Six mice were kept in one cage; 4 such groups were simultaneously injected with a given dosage using a tuberculin syringe. The mice ranged from 18-22 g in weight; average weight 20 g. The mice were observed periodically and the total number dead at the end of 24 hours was taken as the kill for a given dosage. All of the mice surviving 24 hours recovered (with the few exceptions noted below).

Phthalic Acid. The phthalic acid was given as a saturated solution which was shown to contain 0.01 g of phthalic acid per ml. Higher doses than 12 mg per mouse were not feasible since this dosage required the intraperitoneal injection of 1.2 ml which is a large volume compared to the size of the peritoneal cavity. Only with phthalic acid were any observed to die later than 24 hours after administration. The deaths in the second day were as follows: with a dose of 6 mg, late deaths, none; with 8 mg, 2; with 10 mg, none; with 12 mg, 2. The dose required to kill the average mouse (L.D. 50) was calculated† to be 0.55 g per kg body weight (Table 1A). There was some cyanosis noted; the mice hopped about spasmodically, standing

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1 St. George, *Am. J. Clin. Path.*, 1931, **7**, 69.

2 McNally, *Ind. Med.*, 1938, **7**, 295.

3 Blickensdorfer and Templeton, *Am. Pharm. Assn.*, 1930, **19**, 1179.

4 Flury and Wirth, *Arch. Gewerbepath. Gewerbehyg.*, 1933, **5**, 1.

5 Martin and Salmon, *J. Agric. Sci.*, 1934, **24**, 469.

6 Donley, *J. Ind. Hyg. Toxic.*, 1937, **7**, 69.

† The statistical procedure was taken from Bliss, *Ann. Appl. Biol.*, 1935, **22**, 134.

on their hind legs. In certain mice, autopsy showed an apparent subcutaneous hemorrhage in the nasal region; the livers exhibited white spots of unknown etiology.

Sodium Phthalate. The average fatal dose was calculated as 2.1 g per kg body weight (Table 1B); this represents a reduction of toxicity as compared to phthalic acid of about 75%. Cyanosis, convulsive movements and hopping were observed in the treated mice. On autopsy, many mice exhibited congested lungs, hemorrhages into the nasal and oral cavities and pale livers.

Dimethyl Phthalate. The dose required to kill the average mouse was calculated to be 2.4 ml per kg body weight (Table 1C). It was noted that after injection of dimethyl phthalate the mice uniformly developed a marked cyanosis. Their breathing became very rapid

TABLE I.
Data on Dosage and Percentage Mortality.

No. mice	Dosage	No. dead	Mortality %
	A—*Phthalic acid:* 113 mice.		
24	6 mg	1	4
24	8	11	44
41	10	19	46
24	12	12	50
For probit kill—5.00, L.D. 50—11 mg.			
	B—*Sodium phthalate:* 168 mice.		
24	27 mg	4	17
24	33	5	21
24	40	13	54
24	47	13	54
24	53	20	83
24	60	16	67
24	67	20	83
For probit kill—5.00, L.D. 50—42 mg.			
	C—*Dimethyl phthalate:* 120 mice.		
24	.03 ml	0	0
24	.04	7	29
24	.05	13	54
24	.06	19	79
24	.07	24	100
For probit kill—5.00, L.D. 50—0.047 cc.			
	D—*Di n-butyl phthalate:* 97 mice.		
30	.05 ml	1	3
30	.10	13	43
25	.15	25	100
6	.20	6	100
6	.40	6	100
For probit kill—5.00, L.D. 50—0.11 cc.			
	E—*Dioctanol 2 phthalate:* 72 mice.		
24	.5 ml	4	17
24	.8	7	29
24	1.0	15	62
For probit kill—5.00, L.D. 50—0.92 cc.			

and they developed so severe a weakness that they were unable to walk. They became stuporous and remained quiet for some hours.

Di-n-butyl Phthalate. The L.D. 50 was found to be 5.5 ml per kg body weight (Table 1D).

Dioctanol 2 Phthalate. It was found by statistical analysis that the lethal dose for the average mouse is 46 ml of dioctanol 2 phthalate per kg body weight (Table 1E). The mice lived for several hours before any died.

Summary. The L.D. 50 doses for the mice used are as follows: Phthalic acid, 0.011 g; sodium phthalate, 0.042 g; dimethyl phthalate, 0.05 ml; dibutyl phthalate, 0.11 ml; and dioctanol 2 phthalate, 0.92 ml. Compared to phthalic acid, the L.D. 50s of the compounds are as follows: Phthalic acid, 1, sodium phthalate, 4; dimethyl phthalate, 5; dibutyl phthalate, 10; dioctanol 2 phthalate, 84.

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Bomskov Reports on Thymus Mediation of Pituitary Function.

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A series of papers by Bomskov and coworkers[1-5] in Freiburg reports the preparation and extensive investigation of an ether-soluble extract of the thymus. This extract was said to be "diabetogenic" (in rats, guinea pigs, pigeons) in that it showed marked glycogenolytic and hyperglycemic actions. These investigators claimed that a diabetogenic fraction of the anterior pituitary gland failed to lower the liver glycogen in rats whose thymus tissue had been destroyed by Roentgen irradiation.[1] They, therefore, postulated, and later claim to have shown, that the diabetogenic pituitary fraction is thymotrophic and exerts its recognized physiologic actions through stimulating the production of a hormone in the thymus. As the result of other work Bomskov and coworkers[2, 3] indicate that their diabetogenic-thymotrophic fraction from the pituitary gland is identical with growth hormone, and that physiologic effects of the latter

1 Bomskov, C., and Sladovic, L., *Deutsch. Med. Wochschr.*, 1940, **66**, 589.

2 Bomskov, C., and Hölscher, B., *Z. Klin. Med.*, 1940, **137**, 745.

3 Bomskov, C., and Sladovic, L., *Pfluger's Arch.*, 1940, **243**, 611.

4 Bomskov, C., and Brachat, F., *Endokrinologie*, 1940, **23**, 145.

5 Bomskov, C., and Karl-Heinz, K., *Pfluger's Arch.*, 1940, **243**, 623.