## 9640 P

## Toxicity of Sulfanilamide and Diethylene Glycol.

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Sulfanilamide has gained some prominence in the treatment of various infections caused by the gonococcic, meningococcic, and streptococcic organisms. However, the recent deaths caused by the administration of an elixir made from this drug dissolved in diethylene glycol has cast some doubt on its availability as a therapeutic agent. Some 75 deaths have been reported from the use of this so-called elixir.

Toxicity tests were conducted separately with the sulfanilamide and diethylene glycol by using white rats approximately 4 weeks old and weighing from 45 to 60 gm. A mixture of these two substances was also used in the tests. Oral and intraperitoneal administrations were used.

The toxic dose of the diethylene glycol in the preliminary experiments was found to be around 12,500 mg. per kilo of body weight when given intraperitoneally. The oral doses to produce death were approximately the same. Recently, several investigators[1, 2, 3] have found diethylene glycol to be toxic for small animals. The toxic doses of the sulfanilamide were approximately 2600 mg. per kilo of body weight.

An elixir was prepared containing the same amounts of the two principal ingredients as the Elixir of Sulfanilamide-Massengill.[4] This elixir contained 40 grains of sulfanilamide per ounce of a solvent containing 72% diethylene glycol by volume. The results obtained with the elixir paralleled very closely those reported by Geiling, Coon, and Schoeffel.[5] The heating of the elixir for 30 minutes at 95°C. did not change the toxicity. The elixir containing given amounts of sulfanilamide appeared to be more toxic than the sulfanilamide alone. Various doses up to 200 mg. of sulfanilamide per kilo were given orally 3 times a day for 10 days. The results obtained confirmed those of the above-mentioned investigators.

1 Hanzlik, P. J., Seidenfeld, M. A., and Johnson, C. C., *J. Pharm. and Exp. Therap.*, 1931, **41**, 387.

2 Haag, H. B., and Ambrose, A. M., *J. Pharm. and Exp. Therap.*, 1937, **59**, 93.

3 Holck, H. G. O., *J. Am. Med. Assn.*, 1937, **109**, 1517.

4 Editorial, *J. Am. Med. Assn.*, 1937, **109**, 1367.

5 Geiling, E. M. K., Coon, J. M., and Schoeffel, E. W., *J. Am. Med. Assn.*, 1937, **109**, 1531.

In order to render the sulfanilamide more soluble, molecular quantities of hydrochloric acid were added to the sulfanilamide and the mixture was heated for 2 minutes. Various amounts of this hydrochloride were injected intraperitoneally into white rats. The results are given in Table I.

TABLE I.
Toxicity of the Hydrochloride of Sulfanilamide When Administered Intraperitoneally.

| Dose mg./kg. | Male Rats | | Female Rats | | % Mortality |
|---|---|---|---|---|---|
| | Lived | Died | Lived | Died | |
| 200 | 1 | 0 | | | |
| 300 | 1 | 0 | | | |
| 350 | 5 | 2 | | | 28 |
| 400 | 5 | 2 | 3 | 1 | 27 |
| 450 | 4 | 2 | 4 | 2 | 33 |
| 500 | 5 | 2 | 4 | 2 | 31 |
| 600 | 1 | 2 | 2 | 1 | 50 |
| 700 | 1 | 1 | | | 50 |
| 800 | 0 | 3 | 1 | 2 | 83 |
| 900 | 0 | 2 | 1 | 2 | 80 |
| 1000 | 0 | 1 | 0 | 1 | 100 |

The outstanding conclusion to be drawn from the results in Table I is that the hydrochloride is about 4 times as toxic as the base. These results may be explained on the basis of the increased solubility of the hydrochloride.

## 9641 P

## Bodily Electrical Potential Changes Associated with Ovulation and Early Pregnancy in the Chimpanzee.*

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Recently Burr and associates[1] discovered that ovulation in the rabbit is accompanied by large increases in electrical potential. Observations on women, using the apparatus and technique described by Burr, Lane, and Nims,[2] have been reported by Burr and Mussel-

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1 Burr, H. S., Hill, R. T., and Allen, E., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 109.

2 Burr, H. S., Lane, C. T., and Nims, L. F., *Yale J. Biol. Med.*, 1936, **9**, 65.