Evipal by locally retarding its absorption is untenable in view of the similarity of the results (Table I.) obtained for epinephrine by intraperitoneal and intramuscular routes of administration. The insulin-pretreated mice slept slightly longer than those treated with epinephrine. In the dosage employed (0.05 U) there were no convulsions on awakening or other untoward signs. These findings are of interest since the two agents are chemically unrelated and are both normally produced in the body. An extension of the present study is being planned to supply information regarding mechanisms of action. In this connection it is of interest to note that epinephrine has been reported to have an analgesic action in man and in animals.[7]

Summary. White mice pretreated either with epinephrine or insulin and subsequently given Evipal slept considerably longer than the control animals receiving only Evipal. The results are highly significant as determined by statistical analysis.

[7] Ivy, A. C., Goetzl, F. R., Harris, S. C., and Burrill, D. Y., *Quarterly Bull. Northwestern University Medical School*, 1944, **18**, 298.

14900 P

Penicillin as a Prophylactic in Abdominal Surgery.*

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This investigation was undertaken to study the prophylactic value of penicillin in abdominal surgery by depositing penicillin† in the peritoneal cavity and determining the absorption rate of penicillin from the peritoneum into the blood stream.

Material and Method. Seven unselected cases were chosen for this experiment.

Case 1. Clean peritoneum, multiple fibroids. Supracervical hysterectomy and bilateral salpingo-oophorectomy.

Case. 2. Many pelvic adhesions, multiple fibroids. Supracervical hysterectomy and bilateral salpingo-oophorectomy.

Case 3. Ascites, tuberculous. Biopsy.

Case 4. Fibroid, enlarged uterus, 4 months gestation. Myomectomy and hysterectomy.

Case 5. Marked adhesions, old tubal infection, multiple fibroids. Supracervical hysterectomy and left salpingo-oophorectomy.

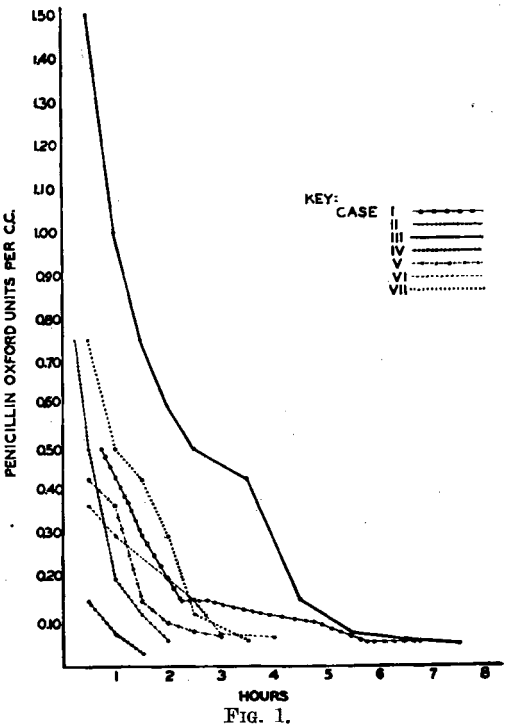

FIG. 1.

Blood level determinations after instillation of 100,000 Oxford units of penicillin into the peritoneal cavity.

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† We are indebted to Mr. John L. Smith of the Charles Pfizer Company, Brooklyn, N. Y., who supplied the penicillin used in this study.

Case 6. Twisted pedunculated fibroid. Myomectomy.

Case 7. Ovarian cyst, clean peritoneum. Left cystectomy.

All these patients received at the end of the operation one hundred thousand Oxford units of penicillin in 20 ml normal saline solution instilled into the peritoneum. Blood was drawn half hourly and hourly up to 8 hours for serum penicillin assays in order to estimate its rate of absorption. The blood was allowed to clot and stored in the refrigerator over night. The penicillin levels were determined by the method of Rosenblatt, Alture-Werber *et al.*[1]

Results. It can be seen from Fig. 1 that the absorption of the instilled penicillin from the peritoneum into the blood stream takes place over a longer period and is more sustained than the intramuscular or the fractional intravenous routes. Peak levels are reached 30 minutes after instillation. Amounts of penicillin sufficient to combat penicillin sensitive organisms are found 3 (Cases 5, 6, 7) to 7 (Cases 1, 3) hours after administration. Case 3 with ascites and a tuberculous process attained the highest blood levels (1.5 Oxford units per ml of serum) and 0.05 Oxford units per ml were present even 7½ hours after the peritoneal deposition.

Summary. Penicillin given by the intraperitoneal route in a single dose of one hundred thousand Oxford units is detectable in the blood stream 3 to 7 hours in 5 cases, and one to 2 hours in 2 cases in sufficient amounts to neutralize penicillin sensitive invaders in abdominal surgery.

[1] Rosenblatt, Philip, Alture-Werber, Erna, Kashdan, Florence, and Loewe, Leo, *J. Bact.*, 1944, **48**, 599.

14901

Chronic Oral Toxicity of Choline Chloride in Rats.*

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The demonstration of the ability of the rat to metabolize relatively large single doses of choline chloride[1] led to an attempt to discover what limits of tolerance exist for chronic administration. Two series of experiments were therefore carried out, (a) in which choline chloride at various levels was incorporated in the solid diet and (b) in which solutions of choline chloride were substituted for the drinking water.

Choline Chloride in Food. Choline chloride at levels of 0.01, 1, 2, 7, 5, and 10% of the diet was fed for periods of 3 to 4 months to groups of 5 rats each. The average body weight curves (Fig. 1) demonstrated that choline at 0.01 and 1% of the diet produced no effect on growth as compared to litter mate controls. 2.7% of choline reduced growth by about 20%, 5% of choline by about 45%, and 10% of choline in the diet permitted no growth.

Food intakes were measured daily for each group over an 8-week period (Table I., A). The lower growth rates in the groups on higher choline intakes were not a result of any specific toxic effect but were evidence of a refusal of food.

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[1] Hodge, H. C., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 26.