

SCIENTIFIC PROCEEDINGS.

VOLUME XXIII.

NOVEMBER, 1925.

No. 2.

New York Meeting

Rockefeller Institute, November 18, 1925.

2838

Phenoltetrachlorphthalein test of a liver function in Eck fistula dogs kept upon meat diet.

BENJAMIN N. BERG, WILLIAM V. CONE and JAMES W. JOBLING.

[From the Department of Pathology, College of Physicians and Surgeons, Columbia University, New York City.]

The chemical studies of phenoltetrachlorphthalein by Orndorff and Black¹ in 1909 were followed by the pharmacological investigations of Abel and Rowntree² in the same year. Subsequently, in 1913, Whipple, Peightal and Clark³ studied the excretion of the dye under experimental conditions. Included among the various types of liver injuries which they produced in dogs were three Eck fistulas. In one of the dogs, the phthalein output was not impaired at the end of twenty-three days after the establishment of the fistula; in another, there was no impairment at the end of one year; in the third, the excretion was low for some weeks after the operation but reached normal values at the end of four months. The determinations were made by the cumbersome and inaccurate method of recovering the dye from the feces and

¹ Orndorff, W. R., and Black, J. A., *Am. Chem. J.*, 1909, xli, 349.

² Abel, J. J., and Rowntree, L. G., *J. Pharmacol. and Exper. Therap.*, 1909, i, 231.

³ Whipple, G. H., Peightal, T. C., and Clark, A. H., *Bull. Johns Hopkins Hosp.*, 1913, xxiv, 343.

urine during a period of twenty-four hours after the injection. Since this work, nothing has appeared in the literature concerning the ability of the liver of Eck fistula dogs to eliminate phenoltetrachlorphthalein.

In 1922, Rosenthal⁴ introduced a simpler and more accurate method of estimating liver function by determining the rate of removal of phenoltetrachlorphthalein from the blood stream. This method was employed in the following study upon Eck fistula dogs.

Seven dogs were used in the experiment. First, an anastomosis was made between the vena cava and the portal vein. Then, the portal vein was ligated above the anastomosis and above the entrance of the vena pancreatico-duodenalis.

The technique* which was employed was a modification of Eck's⁵ original operation described by Guleke,⁶ and Bernheim and Voegtlin.⁷

The test was performed according to Rosenthal's description, at periods varying in the different dogs from forty-six to one hundred thirty-six days after the establishment of the fistulas (see chart). During the twenty-four hours immediately preceding the test, the dogs received no food. Water was allowed *ad libitum*. Six cubic centimeters of blood were withdrawn from one jugular vein for the standard of comparison and then five milligrams of the di-sodium salt of phenoltetrachlorphthalein per kilo of body weight were injected into the same vein. Fifteen minutes and again one hour after the injection, six cubic centimeters of blood were removed from the other jugular vein and the amount of the dye retained in the serum was determined by comparison with colormetric standards.

⁴ Rosenthal, S. M., *J. Pharmacol. and Exper. Therap.*, 1922, xix, 385.

* The surgical procedures were performed in the laboratory of the Department of Experimental Surgery of the College of Physicians and Surgeons.

⁵ Eck, von N., *Militär-med. Journ.*, 1877, lv, 130.

⁶ Guleke, N., *Ztschr. f. Exper. Path. u. Therap.*, (Berlin) 1906, iii, 706.

⁷ Bernheim, B. M., and Voegtlin, C., *Bull. Johns Hopkins Hosp.*, 1912, xxiii,

PHENOLTETRACHLORPHTHALEIN TEST OF LIVER FUNCTION 83

Dog Number	*Per cent of dye in blood serum at the end of 15 minutes.	*Per cent of dye in blood serum at the end of one hour.	Duration of Eck fistula at time of test. Days	Days on meat diet at time of test.	Total duration of Eck fistula at time of autopsy.
I	4%	3%	136	84	155
II	4%	4%	119	86	136
III	3%	3%	114	73	124
IV	4%	3.5%	102	71	166
V	2%	3%	99	78	(no autopsy) 136
VI	3%	3%	71	70	159
VII	3%	3%	46	36	130

* We are indebted to Dr. L. Bauman for corroborating these determinations in his laboratory at the Presbyterian Hospital.

As indicated in the chart, the quantity of the dye recovered from the blood serum at the end of fifteen minutes varied between two and four per cent. At the end of one hour the amount was from three to four per cent. These results are within the range of normal values. They indicate that the rate of disappearance of the phenoltetrachlorphthalein was rapid and that the ability of the liver to remove the dye from the blood was not impaired.

The dogs were kept upon a diet of lean meat which was started at intervals of one to fifty-two days after the operation, and was continued up to the time of exitus. Contrary to the observations of Pawlow and his co-workers,⁸ Fischler,⁹ and others, none of the dogs in the above series exhibited nervous symptoms.

Dogs III, IV, V, and VI became greatly emaciated and died one hundred and twenty-four to one hundred and sixty-six days following the establishment of the Eck fistula (see chart); Dog VII, which had lost considerable weight, was killed after one hundred and thirty days because of mange. Dogs I and II were used for other purposes after the dye injection; subsequently they were killed and examined.

Autopsies were performed upon all of the dogs except dog IV. Examination uniformly revealed that communications had been established between the vena cava and the portal vein, and that the latter had been completely occluded above the entrance of the vena pancreatico-duodenalis. There were no collaterals. The

⁸ Hahn, M., Massen, O., Nencki, M., and Pawlow, J., *Arch. f. Exper. Path. u. Pharmacol.*, 1893, **xxxii**, 161.

⁹ Fischler, F., *Deutsch. Arch. f. Klin. Med.*, 1911, 104, 300.

livers of the Eck fistula dogs showed definite changes which will be described later.

Conclusions. The ability of the liver to remove the di-sodium salt of phenoltetrachlorophthalein from the blood stream was not impaired by the establishment of Eck fistulas in dogs. Definite lesions in the liver (to be described later) followed the establishment of the fistulas. A prolonged meat diet did not induce toxic symptoms in these dogs.

2839

Antiscarlatinal serum of dual potency.

W. H. PARK and A. W. WILLIAMS.

[*From the Bureau of Laboratories, Department of Health,
New York City.*]

The question of the complex nature of hemolytic streptococcus antiserum has been studied since the time of Van deVelde,¹ Marmorek² and others.

Protective power was early demonstrated. Antitoxic powers were also demonstrated broadly for the scarlet fever strains by Moser,³ Savchenko⁴ and others, and were recently made clear cut by the work of Dochez⁵ and of the Dicks.⁶

Realizing that a serum having the power to protect against the living culture, as well as, to neutralize the toxin, might have advantages over a strictly antitoxic serum, we have been inoculating several of our horses by what must be called a modified Moser method. The modifications have been learned by our work on diphtheria antitoxin and antipneumococcus serum, that is, that a protective serum is obtained most easily by the repeated inoculation of the whole killed culture into the vein, and that the antitoxin serum is obtained by the repeated inoculation of toxin subcutaneously.

¹ Vandeveld, *Arch. de Med. Exp.*, 1897, ix, 835.

² Marmorek, Alexandre, *Am. de L' Inst. Past.*, 1895, ix, 593.

³ Moser, *Wien. Klin. Woch.*, 1902, xv, 1053.

⁴ Savchenko, *Russk. Vrach.*, 1905, xxv, 797.

⁵ Dochez, A., *J. Am. Med. Ass'n.*, 1924, lxxxii, 542.

⁶ Dick, G. F., and G. H., *J. Am. Med. Ass'n.*, 1924, lxxxii, 1246.