

7931 P

Phenol Red Clearances in Man.

WILLIAM GOLDRING, ROBERT W. CLARKE AND C. WELSH. (Introduced by H. W. Smith.)

From the Department of Physiology, New York University, College of Medicine, and the Medical Service, Third (New York University) Medical Division of Bellevue Hospital, New York City.

Although phenol red, introduced by Rowntree and Geraghty in 1912, has been widely used as an empirical renal function test in man, there is no information on the excretion of this substance in relation to the simultaneous excretion of other urine constituents.* With knowledge available concerning the order of magnitude of glomerular filtration in man,¹ a determination of phenol red clearance is of particular interest in indicating the relative rôle played by filtration and secretion in the excretion of this substance.

Preliminary observations following oral, intramuscular and intravenous administration of phenol red indicate that the latter is most suitable for investigative purposes. In the observations reported here, a sterile 10% solution of the dye, prepared for us by Hynson, Westcott and Dunning, was administered intravenously following the intravenous administration of inulin, and the experiments were so conducted that the simultaneous clearances of inulin and phenol red could be determined at various plasma levels of the latter, standard (basal) physiological conditions being maintained throughout. The dose of phenol red was varied from 300 mg. to 5 gm. per man, and observations were made at plasma concentrations ranging from 0.1 to 28.2 mg. %.

At plasma levels of the dye below 1.5 mg. %, the phenol red clearance is essentially constant, having an average value of about 400 cc. per minute, when calculated upon the total dye in the plasma. The phenol red/inulin clearance ratio averages about 3.2 under these conditions. A series of such observations on several individuals are recorded in the upper right hand corner of Fig. 1. As the plasma level of the dye is increased, the phenol red clearance is lowered both absolutely and relative to the inulin clearance, until the phenol red/inulin clearance ratio may be less than 1.00. This depression of the phenol red clearance appears to be reversible, the

* MacKay, E. M., (PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 1039) has reported three observations on the relative ratio of excretion of phenol red and urea in man.

¹ Shannon, J. A., and Smith, H. W., *J. Clin. Invest.*, in press.

same results being obtained, whether an intermediate plasma concentration is reached by the administration of a small dose, or on a falling plasma curve after the administration of a large dose. Results obtained in two series of observations on one individual (L.R.) are recorded in the figure.

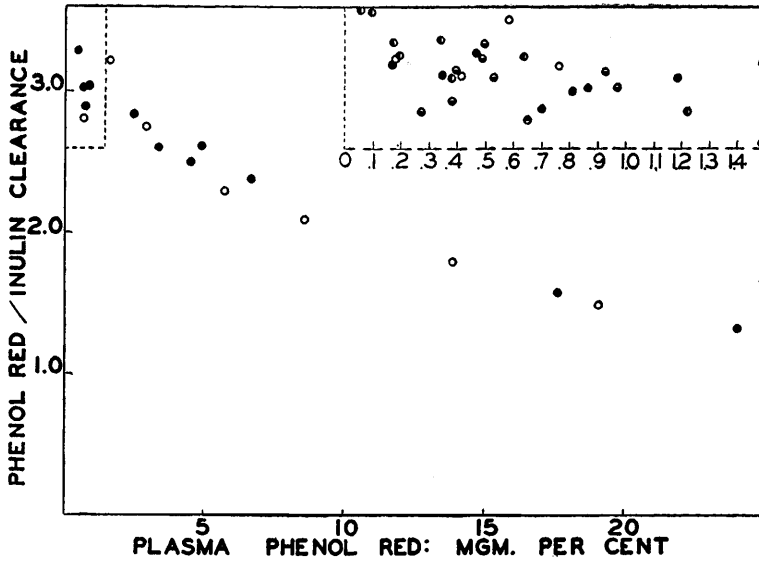


FIG. 1.

The magnitude of the phenol red/inulin clearance ratio, as well as the curvilinear relationship between plasma concentration and rate of excretion, indicates that the greater proportion of the dye is excreted by a process of tubular secretion. At 2.5 mg. % in L.R.'s plasma (35 mm. p CO₂ and 37.5°C.), 23% of the dye was filtrable through collodion. This figure is probably slightly less at lower plasma levels, but granting that filtration cannot account for the excretion, relative to the inulin clearance, of a greater fraction of the total plasma dye than this, it follows that about 8% of the dye appearing in the urine is excreted by filtration and 92% is removed from the post-glomerular blood and transferred to the tubular urine by tubular activity. At very low plasma levels (such as are obtained with the routine phenol red test) the fraction of dye excreted by tubular activity must be at least this large. If phenol red were excreted solely by filtration there would be required, when allowance is made for the small fraction of filtrable dye, 2000 cc. of filtrate per minute, which is considerably in excess of the probable blood flow to the kidneys.

The relations existing in man between plasma level and rate of excretion are entirely similar to those described in the dog by Shannon in the accompanying paper, except that at all plasma levels the phenol red clearance in man is relatively much greater than the inulin clearance. In man the maximal phenol red/inulin clearance ratio is 3.2 as compared to 1.7 in the dog. When one takes into account the fact that there is about twice as much free phenol red in dog's plasma as there is in man's, this difference becomes all the more significant in indicating a great difference in the capacity of the two kidneys to secrete this substance.

7932 C

Effect of Splenectomy on Bacterium Enteritidis Infection in White Mice.

JESSIE MARMORSTON

From the Department of Pathology of Cornell Medical College, New York City.

It has been well established that removal of the spleen in many species of animals depresses the natural resistance to certain bacterial, protozoan and spirochetal infections.* The rôle of the spleen in the maintenance of an acquired resistance to latent piroplasmidae and bacterial infections has been demonstrated in *Bartonella muris* infection in the rat, in *Bartonella canis* infection in the dog, in *Eperythrozoon coccoides* and *Bartonella muris* infection in the mouse, in infection with *Nuttalia equi* in the horse, Anaplasmosis in sheep and cattle and *Babesia bigeminum* in cattle.³ Removal of the spleen converts a latent infection into manifest disease, often associated with a severe fatal anemia.

Morris and Bullock studied a spontaneous epizootic infection, with *Bacterium enteritidis* (Gaertner), in their rat colony and noted that splenectomy conspicuously lowers the resistance of the rat to this natural infection.⁴ They were unaware, however, of the occurrence

* The relation of the spleen to resistance has been discussed in papers of Perla and Marmorston,¹ Marmorston², and in a recent monograph.³

¹ Perla, D., and Marmorston-Gottesman, J., *J. Exp. Med.*, 1930, **52**, 601; 1931, **53**, 869, 877.

² Marmorston, J., *J. Inf. Dis.*, in press.

³ Perla, D., and Marmorston, J., *The Spleen and Resistance*, Williams and Wilkins, Baltimore, 1935.

⁴ Morris, D., and Bullock, F., *Ann. Surg.*, 1919, **70**, 513.