tion. A similar relationship has been found in man. Typical examples are presented in Fig. 1. The large difference in the values of the ratios: $\frac{\text{Urine rate}}{\text{Plasma concentration}}$ is undoubtedly due, as in the case of urea,[1] to the different amounts of renal tissue possessed by man and the rabbit. Under the same conditions urea behaves in a like manner[2] although the urine rate for a given plasma concentration is always greater for creatinine. That is, the excretory ratio $\frac{\text{Urine rate}}{\text{Plasma concentration}}$ is less for urea. The significance of this will be discussed elsewhere. Since the difference between the ratios for these 2 substances appears to bear a constant relation to the lower it is obvious that creatinine may be substituted for urea in measuring renal function by Addis' method.[3] Rehberg[4] has used creatinine in what is essentially this method but failed to observe the standard or other constant conditions and obtained inconstant results. He found[5] only a general tendency for the urine rate to increase in proportion to the plasma concentration. An examination of the method using creatinine under more rigid conditions is now in progress.

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Bacteriostatic Action of Dyes on the Organisms of Undulant Fever.

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As one of the various means purported to differentiate the undulant fever bacteria of caprine, bovine, and porcine types, the inhibitory effect of certain dyes, particularly gentian violet and thionin, has been suggested. As with other means of differentiation, there is no absolute scale for comparison, inasmuch as not all strains fall consistently into any one group by all differentiating tests.[1] The present study attempts to throw some light on the discrepancies in so far as the bacteriostatic effect of dyes is concerned.

[1] Taylor, F. B., Drury, D. R., and Addis, T., *Am. J. Physiol.*, 1923, lxv, 55.

[2] Addis, T., and Drury, D. R., *J. Biol. Chem.*, 1923, lv, 105.

[3] Addis, T., *Arch. Int. Med.*, 1922, xxx, 378.

[4] Rehberg, P. B., *Zentralbl. f. inn. Med.*, 1929, l, 367.

[5] Rehberg, P. B., *Biochem. J.*, 1926, xx, 447.

[1] Meyer, K. F., and Eddie, B., in press.

The technic, briefly described, consisted of making appropriate dye concentrations in melted liver hormone agar, from which plates were poured, and cultures streaked on a sector from a broth suspension of an agar slant culture, to insure a degree of uniformity in inoculum. The results were most clearly observed after 72 to 96 hours of incubation at 37° C. The cultures used were obtained from Tunis, Austria, Italy, Denmark, Germany, and from the western part of the United States, and represented a variety of animal and human sources.

The correlation between the original sources of cultures and the bacteriostatic effect of gentian violet, basic fuchsin, brilliant green, thionin, and methylene blue, considered individually or collectively, was found to have a number of discrepancies. Gentian violet in dilutions of 1:50,000 allowed growth with some strains, and inhibited completely in a 1:250,000 dilution with others. Basic fuchsin, chemically related to gentian violet, in most instances allowed virtually normal growth in a 1:50,000 dilution, or even lower, but in some instances inhibited completely in a dilution of 1:100,000. Brilliant green possessed a marked inhibitory quality, permitting on occasion a moderate growth in a 1:1,250,000 dilution; other cultures were almost entirely inhibited in a dilution twice as great. Methylene blue and thionin, although chemically related, vary greatly in bacteriostatic action. Methylene blue with most strains completely inhibited in a dilution of 1:1,000,000, although some growth occurred with several strains. Thionin, on the other hand, permitted vigorous growth in a dilution of 1:25,000 in some instances, although a 10-fold dilution inhibited other strains.

Four samples of thionin, from 3 manufacturers, showed a marked divergence in bacteriostatic action. For example, 40% of the strains tested were completely inhibited in a 1:250,000 dilution of one dye sample, whereas another sample showed no inhibition in any instance in this dilution. The latter required a concentration approximately 5 times as great in order to inhibit in the same percentage of cultures tested as the former sample, and the inhibited strains were not the same.

The quantity of inoculum influences the degree of inhibition by dyes. It was found possible to obtain growth in dye concentrations 5 to 10 times as great as those ordinarily inhibiting by the use of a reasonably heavy inoculum from a slant culture.

The specific stability of bacteriostatic action shows little, if any, variation, as tested with the same cultures over a period of one year.

Among other apparently demonstrable vagaries in dye inhibition of this group of organisms, perhaps one of the most important is the stage of development of the particular strain. The rough, or R, type of colonial growth appears in most instances tested to be definitely more resistant to bacteriostatic action than does the smooth, or S, type. Comparative growth of S and R growth on the same dye plates frequently reveals striking differences. Inasmuch as the S and R forms, although relatively stable, are at no time perfectly stable, this seems an additional source of difficulty or of error in the utilization of bacteriostatic action as a means of type differentiation.