

ileum of 2 patients with intestinal obstruction. The figures for sodium chloride were calculated from the chloride determinations as if all the chlorine were present as sodium chloride.

The point we wish to emphasize is that excepting 2 instances (sodium in patients 21 and 22) the concentration of sodium chloride in the gastro-intestinal secretions examined was always less than the concentration of sodium chloride in physiological saline or Ringer's solution.

This suggests for patients losing gastro-intestinal secretions and requiring fluids parenterally that the sodium chloride lost may be replaced by giving a volume of physiological saline or Ringer's solution equal to the volume of gastrointestinal secretion lost. The possibility of preventing a deficiency of sodium chloride by this volume for volume rule is being investigated now in a series of surgical patients.

9555

Toxicity of meta-Substituted Phenols to *Paramecium caudatum*.

EDWIN H. SHAW, JR., AND LEO J. GEPPERT. (Introduced by I. N. Kugelmass.)

From the Department of Biochemistry, University of South Dakota Medical School.

The duration of life of individual paramecia was measured at various concentrations of antiseptic agents, at $25 \pm 1^\circ\text{C}$., and at pH 7.6. Duplicate runs were made on separate pure cultures of *Paramecium caudatum*, using an average of 20 organisms at each concentration in each run. The solution of the toxic agent and the 0.5% oat straw infusion paramecium culture were measured from microburettes, mixed in small depression slides, and placed in a stage thermostat for microscopic observation. Death was considered to occur when motility ceased. Morphological alterations indicated that the organisms actually were dead, especially the formation of clear spherical blisters about the periphery, the disappearance of the vacuoles, and a darkening and clumping together of the cytoplasmic elements. The death times at each concentration in each run were averaged. The average of the probable error in the death times was 3.3%.

The results of each run on each compound were plotted separately, log c against log t . The straight lines obtained conform to the

Ostwald¹ toxicity equation, $c^n t = k$, where c is the concentration of toxic agent in mols per liter, t is the death time in seconds, and n and k are constants. For each run, n was determined as the slope, $\log t$ divided by $\log c$, of the balanced line drawn through the points. The 2 values of n obtained for each compound were averaged and the probable error in n was expressed statistically, averaging 2.8%. From the average value of n for a given compound, k was calculated by substitution in the equation for all the points in both runs, and the probable error in the average k was expressed statistically, averaging 3.6%. From the average values of n and k , the straight lines in Fig. 1 and 2 were drawn. The points are the average of the death times in the 2 runs.

The numerical values of the constants, n and k , are given in Table I. The 2 constants may be combined into a single constant, the n th

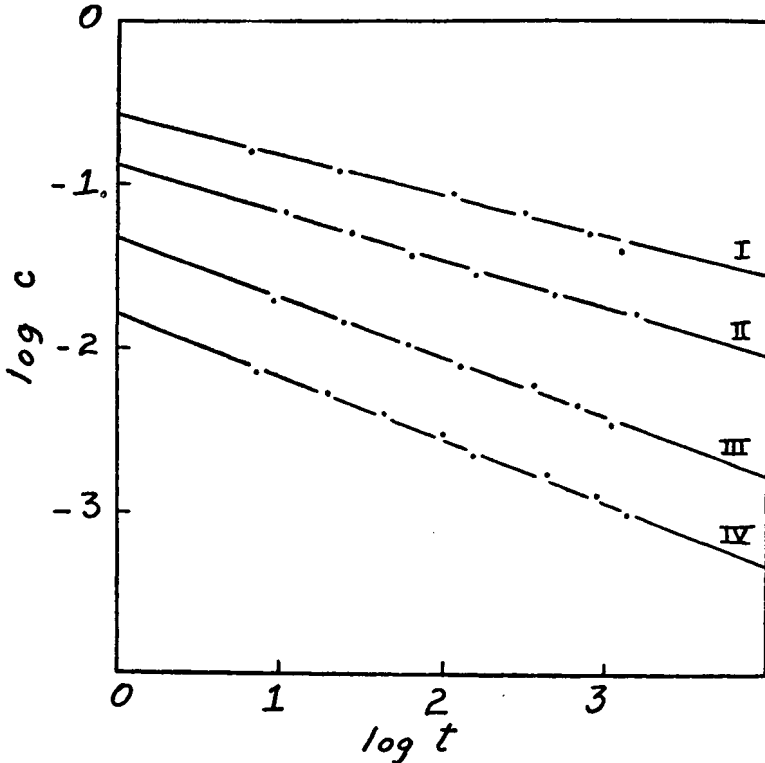


FIG. 1.

Kinetics of death of *Paramecium caudatum* under the influence of: I. m-amino-phenol; II. Resorcinol; III. Resorcinol monomethyl ether; IV. m-nitro-phenol.

¹ Ostwald, Wo., *Arch. ges. Physiol. (Pfluger's)*, 1908, 120, 19.

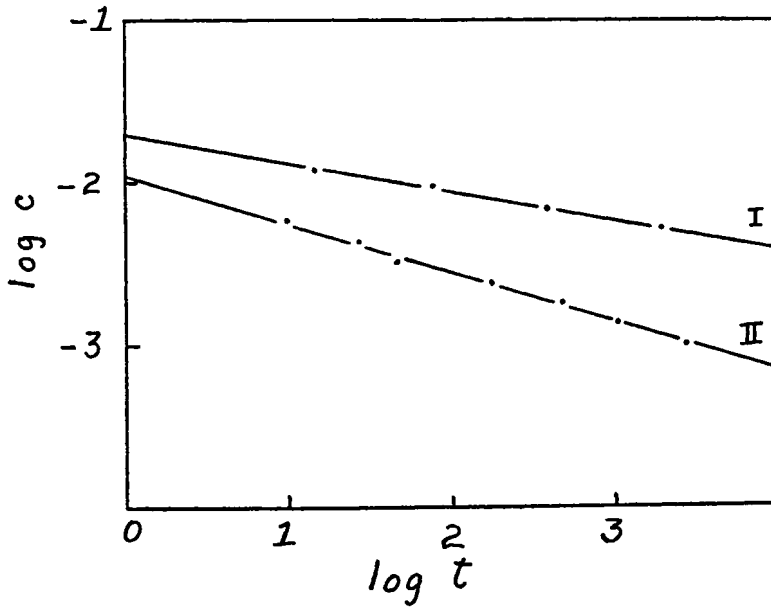


FIG. 2.

Kinetics of death of *Paramecium caudatum* under the influence of: I. m-cresol; II. m-chloro-phenol.

root of k , which is the concentration of toxic agent required to bring about death in unit time, one second. The n th root of k might be called the *Toxicity Coefficient*. Since surface tension might be considered the cause of death, the surface tension, of the highest concentration of each toxic agent used, was measured by the Du Nuoy method. The surface tension, in all cases, was within the range of surface tension that was normal for the oat straw infusion cultures used, 62.8 to 72.1 dynes per cm.

Inspection of Table I shows a relatively wide range of variation

TABLE I.
The Constants, n and k , in the Ostwald Toxicity Equation.

| Compound | n | k | Toxicity Coefficient $\sqrt[n]{k}$ | Surface Tension of strongest soln. dynes/cm. |
|------------------------------|----------------|--------------------------------|---------------------------------------|---|
| m-chloro-phenol | $3.37 \pm .02$ | $2.50 \pm .11 \times 10^{-7}$ | .0109 | 72.5 |
| m-nitro-phenol | $2.63 \pm .3$ | $2.01 \pm .05 \times 10^{-5}$ | .0164 | 72.8 |
| m-cresol | $5.71 \pm .02$ | $1.80 \pm .02 \times 10^{-10}$ | .0196 | 64.5 |
| Resorcinol mono-methyl ether | $2.73 \pm .07$ | $2.44 \pm .09 \times 10^{-4}$ | .0475 | 65.1 |
| Resorcinol | $3.42 \pm .03$ | $9.99 \pm .23 \times 10^{-4}$ | .1328 | 69.2 |
| m-amino-phenol | $4.15 \pm .03$ | $3.99 \pm .30 \times 10^{-3}$ | .2646 | 65.2 |

in the constants n and k for this closely related group of compounds. With the constituents arranged in increasing order of the n th root of k or decreasing antiseptic efficiency, as above, it is interesting to note that Labes and Jansen² arranged the substituents in phenol in the same order of decreasing ability to coagulate serum albumin, chloro, nitro, methyl, hydroxyl, indicating a definite parallelism between antiseptic efficiency and ability to coagulate proteins. This parallelism gives supporting evidence to Bancroft's³ colloidal coagulation theory of disinfectant action. An analogy can be shown between the Ostwald toxicity equation and the Ishizaka⁴-Gann⁵ equation for the kinetics of the coagulation of colloidal $Al(OH)_3$ by KCl

$$t = \frac{2.303}{ac^n(1+b)} \log \frac{b+x}{b(1-x)}$$

where x is the fraction coagulated in time t when the concentration of KCl is c , the terms a , b , and n being constants. If the time to a given degree of coagulation, t_s , is taken, this equation reduces to $c^n t_s = k$, identical, in form and range of magnitude of n , with the Ostwald toxicity equation. The Ostwald toxicity equation can therefore be considered to measure the time until a sufficient degree of protoplasmic coagulation has occurred to produce death.

Conclusion. Additional evidence is presented to support the Bancroft colloidal coagulation theory of disinfectant action. A new measure of the efficiency of antiseptic agents, the Toxicity Coefficient, is defined on the basis of the Ostwald toxicity equation.

² Labes, R., and Jansen, E., *Arch. exp. Path. Pharm.*, 1930, **158**, 1.

³ Bancroft, W. D., and Richter, G. H., *J. Phys. Chem.*, 1931, **35**, 511.

⁴ Ishizaka, N., *Z. physik. Chem.*, 1913, **83**, 97.

⁵ Gann, J. A., *Kolloidchem. Beih.*, 1916, **8**, 63.