

In vitro Sensitivity of Recently Isolated Cholera Vibrios to Ten Antibiotics. (18752)

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The activity of antibiotics against *Vibrio comma* is usually determined in American and European institutions using relatively old stock strains. *V. comma* cultures maintained in laboratories, however, frequently undergo changes. It was observed during preliminary experiments(1,2) that the susceptibility of these organisms to antibiotics increases during storage. It was decided, therefore, to examine 53 cholera vibrio strains which were received shortly after isolation in Egypt, India and French Indochina, for the estimation of the sensitivity of *V. comma* to antibiotics.

The tube-dilution method was employed in these experiments. Duplicate series, containing decreasing amounts of the respective antibiotics, were set up and inoculated with measured amounts of an 18- to 20-hours-old broth culture. All tests were carried out using Penassay Broth, Difco, and read after 20 to 22 hours incubation at 37°C.

Penicillin G, chloromycetin, neomycin, terramycin, polymyxin D, bacitracin and prodigiosin were received from the Commercial

Solvents Corporation, Terre Haute, Indiana. Penicillin O (Cer-O-Cillin) and streptomycin were supplied by the Upjohn Co., Kalamazoo, Michigan. Aureomycin was furnished by the Lederle Laboratories, Pearl River, N. Y.

The results of these experiments revealed considerable variations in the susceptibility of cholera vibrios to the different antibiotics according to the geographical origin of the strains. Table I, which summarizes the outcome of these tests, shows, therefore, the results with regard to the place wherefrom the vibrios were received.

Cholera vibrios from the Bombay area were susceptible to all antibiotics tested in this series. Ogawa types were, on the whole, somewhat more resistant to antibiotics than Inaba strains. Inaba type organisms from Bombay were less sensitive to neomycin, bacitracin and aureomycin, but more susceptible to terramycin and polymyxin D than strains from other areas. While resistant organisms were not received from Bombay or Egypt, several strains from Bengal and Assam, as well as

TABLE I. *In Vitro* Susceptibility of 53 Cholera Vibrios to Antibiotics According to Geographical Origin.

Strains No. tested From	Inaba 3 Egypt	Inaba 5 Bombay	Ogawa 5 Bombay	Inaba 10 Bengal	Ogawa 10 Bengal	Inaba 10 Indochina	Ogawa 10 Indochina
Antibiotic	Mean inhibitory dose in μ g or units in ml medium						
Penicillin G*	25	20	22.5	35.5†	50.5‡	54.2‡	60.1‡
" O	25	14.5	16.25	30.6†	42.8‡	31.5†	55.7‡
Streptomycin	10.3	25	14.5	28.3†	29.1†	22.5†	30.2†
Chloromycetin	5.3	1.57	3.2	.9†	4.1†	3.7†	3.9†
Aureomycin	.23	2.82	3.4	.7†	4.9†	.4†	.8†
Neomycin*	.36	4.07	4.37	.62	.72	1.62	1.75
Terramycin	2.5	2	3	2.81	3.18	—	—
Polymyxin D*	12.26	1.62	.96	4.32†	6.62†	—	—
Bacitracin	1.5	100 ‡	100 ‡	2.91	4.88	18.5†	22.4†
Prodigiosin	.5	.6	1.12	—	—	—	—

* In units.

— Not tested.

† One to 2 strains resistant to 100 units or μ g.

‡ Three to 5 strains resistant to 100 units or μ g.

1. Felsenfeld, O., Volini, I. F., Ishihara, S. J., Bachman, M. C., and Young, V. M., *J. Lab. and Clin. Med.*, 1950, v35, 428.

2. Felsenfeld, O., Volini, I. F., Young, V. M., and Ishihara, S. J., *Am. J. Trop. Med.*, 1950, v30, 499.

from French Indochina, were not sensitive to most antibiotics in doses smaller than 100 units or μg per ml test fluid. Organisms resistant to neomycin or terramycin were not encountered. The number of strains tested with prodigiosin is small but the results are encouraging.

Summary. Fifty-three recently isolated strains of *V. comma* were tested against 10 antibiotics. The results showed a wide variation of susceptibility to these drugs, according to the geographical origin of the vibrios.

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Some Early Nuclear Effects of Ionizing Radiation.* (18753)

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The cellular changes which follow ionizing radiation have been most extensively investigated in relation to mitoses. It is noted that within 12 minutes after exposure to heavy doses, mitotic inhibition may occur, and the chromosomes involved show clumping, fragmentation and lagging(1). Nuclear chromatin degenerates and giant nuclei may result. These relatively temporary effects are seen particularly in the mitotic prophase, and the different susceptibilities of various cell types is well established. Cytoplasmic alterations such as vacuolization and massing of the Golgi network and fragmentation are observed, but major interest still attaches to nuclear changes. Various mechanisms have been invoked in explanation. The idea that ionizing radiation prevents formation of desoxyribose nucleic acid from ribose nucleic acid, thus inhibiting chromosome synthesis(2), has also some support from investigation of chemical agents which inhibit prophase onset and are hence termed "radiomimetic." According to Dustin(3) these agents produce sequentially (a) cytoplasmic swelling, (b) alteration of nuclear membrane, (c) accumulation of thymonucleic acid on nuclear membrane with fragmentation and disappearance of all

chromosomes, (d) spherical massing of basic protein and ribonucleoprotein, with persisting nucleolus, then (e) rapid fragmentation with extrusion of debris from the cell.

Present studies. As a preliminary to histochemical study of this problem, a series of rats injected intraperitoneally with large doses of P^{32} † were killed at hourly intervals. Lethal radiation effects consisting of nuclear pyknosis and fragmentation were usually observed in lymphoid tissues, intestinal crypts, bone marrow and gonads. In contrast to and at times preceding this lethal type of radiation reaction, nuclear swelling was observed in many tissues. In those sensitive cells mentioned above it proceeded to cell death, whereas in other organs such as liver, kidney and perhaps brain, nuclear swelling disappeared within 24 hours. Thus the more radioresistant tissues appeared to show a nonlethal reversible radiation effect.

With the conventional formalin- or Zenker-fixed paraffin embedded tissues, however, nuclear detail is not adequately preserved to permit of an accurate study and interpretation of such relatively slight nuclear alterations. The simplified freezing-drying technic devised in this laboratory for autoradiography(4), and since used with success in histochemical problems(5), has proved useful in this situation. Feulgen stains of normal and irradiated tis-

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1. Warren, S., *Arch. Path.*, 1942, v34, 443.
2. Koller, P. C., *Brit. J. Radiol.*, 1947, Suppl. No. 1, 84.

3. Dustin, P., *Nature*, 1947, v159, 794.

† The P^{32} used was obtained from the Oak Ridge National Laboratory.

4. Holt, M. W., Cowing, R. F., and Warren, S., *Science*, 1949, v110, 328.