

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY — 1961

Proceedings of the First Interscience Conference on
Antimicrobial Agents and Chemotherapy,
New York City, October 31 — November 2, 1961

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Preface

In any field of scientific endeavor a medium for the mutual exchange of ideas and information among the investigators is both desirable and essential. This is particularly true when the subject of investigation overlaps several related disciplines. In extension of its aim to advance scientific knowledge in microbiology and allied fields, the American Society for Microbiology has embarked upon a program of interscience conferences which are designed to provide the opportunity for intercommunication between microbiologists and investigators in related disciplines. To this end, a Committee on Interscience Conferences, under the chairmanship of Dr. Orville Wyss, has been established and charged with the encouragement and general supervision of conferences of an interdisciplinary nature, independent of the present framework of the Society's Annual Meeting.

The broad area of antimicrobial agents and chemotherapy covers a wide spectrum of research activity in the fields of microbiology, chemistry, pharmacology, biochemistry, clinical medicine, and pathology. Although these disciplines are diverse, they nevertheless are characterized by numerous and varied interrelationships which provide bonds of common interest. In late 1960, in response to a petition by a number of investigators whose interests lie in those several disciplines, the Council Policy Committee of the Society authorized the sponsorship of an Interscience Conference on Antimicrobial Agents and Chemotherapy and assumed the responsibility for publication of the proceedings of the Conference. It is planned that this Conference will be held annually. To insure its permanence on a continuing basis, appropriate mechanisms were set up by the Council Policy Committee.

The first of such conferences was held October 31 to November 2, 1961, the proceedings of which are presented in this *Annual*. The obvious success of this meeting raises the hope that subsequent Interscience Conferences of this or a comparable nature will furnish tangible evidence of the desire of the Society to be of service to microbiologists and their colleagues in related scientific fields.

The Society is deeply indebted to all of the individuals who contributed of their time and effort—through membership on the several committees or through personal service at the time of the meetings—to the effective organization and operation of the Conference. They were ably assisted by the Executive Secretary and the Managing Editor of the Society's headquarters staff. A special word of thanks is due to the Executive Committee of the Conference, which was composed of Dr. George M. Savage (Chairman), Dr. Maxwell Finland, and Dr. John C. Sylvester.

JOHN E. BLAIR, *President*

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NOSOCOMIAL INFECTIONS WITH *HERELLEA* *VAGINICOLA* IN BURNED PATIENTS

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The term "therapy-potentiated infection" is applied to hospital patients in whom intense, protracted antibiotic treatment has resulted in invasion by an organism which normally would not cause disease. It is to be regarded as the price exacted for a necessary and frequently life-saving procedure. These infections are most often caused by commensal organisms which behave as opportunistic invaders. Thus, intestinal candidiasis may follow prolonged oral antibiotic administration.

An alarming development of the past decade of antibiotic therapy has been the appearance of saprophytes which behave as pathogens, probably because of a disturbance of the equilibrium of the microbial flora by antibiotics. Thus, *Bacillus subtilis* (Cox, Soekwell, and Landers, 1959) and *Serratia marcescens* (Graber et al., 1960) have been reported as agents of septicemia in man. The most important member of this group of commensal bacteria is undoubtedly *Pseudomonas aeruginosa*, strains of which have shown a remarkable potentiality for invading severely debilitated patients during prolonged antibiotic therapy. This is especially noteworthy in the seriously burned patient (Rabin, Graber, and Vogel, *in press*; Tumbusch et al., 1961). No antibiotics have yet been shown to cope with such infections.

Bacterial invasion of patients in the burn ward offers an excellent environment for studying therapy-potentiated infection, since the initial open wound, followed by an exuding eschar, calls for intensive antibiotic prophylaxis to avert bacteremia. Under these conditions, our unit has noted the appearance, with increasing frequency, of infections with an organism of obscure taxonomic position, corresponding to the description of *Herellea vaginicola* as given by De Bord (1942). There have probably been other binomials applied to this organism, including the *B. anitratum* of Schaub and Hauber (1948). The *Diplococcus mucosum* of Von Lingelsheim (1905) may have been the same organism. Many European taxonomists appear to favor the classification of *Moraxella lwoffii* (Andreau, 1940). The organisms are gram-negative to gram-variable cocco-bacilli, pleomorphic,

relatively inert toward carbohydrates, and most are probably to be placed in the family *Parvobacteriaceae*, according to the current consensus of taxonomists. A principal biochemical feature is the inability of these organisms to reduce nitrate to nitrite. The ambiguous taxonomic status of these organisms is such that they were omitted from the 7th edition of Bergey's Manual of Determinative Bacteriology.

This report documents the appearance of *H. vaginicola* as a surface contaminant in burn wounds of patients at this unit, its appearance in bacteremia accompanying such infections, and the antibiotic refractoriness of these organisms.

Experimental

Notation of a recovery of a culture of *H. vaginicola* at this unit was first made early in 1960, when positive blood cultures were obtained on three successive days from one patient. No *Herellea* organisms had been reported isolated from burned surfaces or blood cultures prior to this time. After the recognition of the first bacteremic strain, a greater awareness of the possible presence of *H. vaginicola* developed. During the remainder of 1960 and the first 6 months of 1961, cultures from 68 of 133 patients were positive, with a total of 362 isolations being made (Table 1).

TABLE 1. Isolation of *Herellea vaginicola* from burned patients

Year	Surface cultures			Blood cultures	
	Total patients	Patients positive	Total isolates	Antemortem	Postmortem
1960	99	50	260	3	5*
1961	34	18	102	0	0
Total	133	68	362	3	5

*One patient positive antemortem as well as postmortem.

During this period, a total of seven patients yielded positive blood cultures for this organism. Three of these were antemortem, and four postmortem, with one patient positive both ante- and postmortem. Another patient exhibited a positive terminal blood culture, as well as a postmortem positive. The three antemortem patients showed positive cultures on the 4th to 6th, 11th to 16th, and 5th to 8th postburn days, respectively.

All of the patients with positive *Herellea* blood cultures died, but except for one patient, the *H. vaginicola* from the blood stream always accompanied either *P. aeruginosa* or *P. aeruginosa* with yet a third organism. The five postmortem positive blood cultures were usually accompanied by *Pseudomonas*. In two patients with positive

Herellea blood cultures during their illness, administration of colistin sulfate was followed by disappearance of this organism from the blood stream. One of these patients succumbed after several subsequent blood cultures positive for *Pseudomonas*; the second showed mixed *Staphylococcus aureus* and *P. aeruginosa* in the blood stream at death.

H. vaginicola grows well on routine laboratory media, and on blood agar forms large, round, smooth, nonhemolytic, gray colonies. The strains here observed grew well on eosin-methylene blue agar and on MacConkey's agar. The strains fermented glucose, xylose, and arabinose without gas production. Lactose, sucrose, salicin, and mannitol were not fermented in conventional 1% solutions. However, *Herellea* strains exhibited the peculiar ability to ferment concentrated but not dilute lactose, and all strains observed formed acid in 10% semisolid agar. The bacteremic strains were found to agglutinate strongly in antiserum for the Communicable Disease Center (CDC) *H. vaginicola* strain 101. Weak agglutination occurred in antisera for CDC strains 1043, 39, 26, and 969. The strains observed were thus closely related or identical, culturally and serologically, with CDC strain *H. vaginicola* 101.

TABLE 2. Disc and tube sensitivity of *Herellea vaginicola* to selected antibiotics*

Isolates	Pen (10 units)	Chloro (30 µg)	Erythro (15 µg)	Terra (30 µg)	Kanamycin (30 µg)	Neomycin (30 µg)	Poly B (30 µg)	Colistin (30 µg)
362	< 1	45	79	73	96	98	95	93
C.P.†								
(2-7-1)	> 25	> 25	6.2	3.1	6.2	6.2	0.39	0.39
(2-8-2)	> 25	> 25	6.2	3.1	12.5	6.2	0.39	0.39
M.M.†								
(5-22-5)	> 25	> 25	.78	.78	3.1	3.1	3.1	0.78
(5-27-1)	> 25	> 25	.78	.78	6.2	6.2	6.2	0.39
C.S.†								
(5-28-3)	> 25	> 25	> 25	—	3.1	3.1	3.1	1.5
(5-59-1)	> 25	> 25	> 25	> 25	3.1	6.2	12.5	1.5

*The paper-disc method was used to determine the per cent sensitivity of all isolates (first row). Pen = penicillin; Chloro = chloramphenicol; Erythro = erythromycin; Terra = oxytetracycline (Terramycin); Poly B = polymyxin B.

†These bacteremic strains all showed, in addition to the results listed, insensitivity to more than 25 µg streptomycin, vancomycin, and bacitracin. These strains were tested by the tube dilution method; results are in µg/ml.

When tested by the disc method for antibiotic sensitivity, the 362 *H. vaginicola* strains were in the main relatively resistant to penicillin and to the broad-spectrum antibiotics (Table 2). Less than half of the strains were sensitive to chloramphenicol, but three-fourths of the strains were sensitive to oxytetracycline and almost four-fifths were sensitive to erythromycin. Almost all strains were sensitive to kanamycin, neomycin, polymyxin B, and colistin sulfate.

The sensitivity of strains from the three patients with *Herellea* bacteremia during life were studied by tube dilution method. The strains were resistant to penicillin, chloramphenicol, streptomycin, vancomycin, and bacitracin. All were relatively sensitive to neomycin, kanamycin, polymyxin B, and colistin sulfate. Marked variations were noted in sensitivity to erythromycin and to oxytetracycline.

Discussion

Although there have been increasingly frequent reports (Schaub and Hauber, 1948; Weed, 1961) of organisms of the tribe *Mimae* being observed as etiological agents of disease, they are evidently unfamiliar to a relatively large proportion of bacteriologists. The lack of a generally accepted taxonomic position for this group of organisms may account for their omission from the current Bergey's Manual. The belated recognition of *Herellea* in our laboratory emphasizes the need for wider knowledge of these organisms. An appeal for reports of infections due to *Mimae* was recently made by Weed (1961) of the Mayo Foundation.

It is virtually certain that *H. vaginalis* was being overlooked in surface cultures from burned patients in our laboratory prior to 1960. When the organism was found in the blood stream, more detailed study of colonies resembling those of *Enterobacteriaceae* revealed the group to be relatively frequent inhabitants of burned surfaces. The appearance of this organism in bacteremia may connote increased invasive capability on the part of some strains, but is more probably evidence of increasing resistance to antibiotics. The strain was streptomycin-insensitive, and the prophylactic regimen of penicillin and streptomycin which almost all burned patients received during the period of observation may well have contributed to permitting the organism selectively to survive. The strain was indeed a definite invader of the blood stream in at least three patients, since multiple isolations were obtained from each individual during life.

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