The Virulence of Glucose Non-fermentative Organisms In Experimental Pyelonephritis in Mice

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Summary

The virulence of clinical isolates of *Acinetobacter calcoaceticus*, *Pseudomonas cepacia*, and *Pseudomonas maltophilia* in urinary tract in mice was studied. In general, the virulence of these organisms in urinary tract of normal mice was relatively mild. The effect of anti-inflammatory and immunosuppressive drugs on pathogenicity of these organisms was studied in mice. The mice previously treated with betamethasone or prednisolone as anti-inflammatory drug, and with cyclophosphamide or azathiopurine as immunosuppressive drug, were more susceptible to these bacterial infections than were the non-treated ones. As for the capacity of bacterial attachment to the epithelial cells of the bladder, these organisms were generally shown to have low adhesion. Furthermore, the hemagglutination patterns were mannose-sensitive in human and guinea pig erythrocytes.

Introduction

In recent years, glucose non-fermentative rods such as *Pseudomonas* spp., *Acinetobacter* spp., and *Achromobacter* spp. have come to play a significant role in clinical infections¹⁾²⁾. These ubiquitous organisms were originally considered to be nonpathogenic in man. Over the last decade, however, they have been documented as infections, particularly in post-operative and debilitated patients. In addition, long-term treatment with antibiotics or immunosuppressive drugs and the presence of an in-dwelling urethral catheter are regarded as the causative factors for pseudomonal or acinetobacterial infection. The infections due to these bacteria include meningitis³⁾, urethritis⁴⁾, urinary tract infection (UTI)⁵⁾, pneumonia⁶⁾, and septicemia⁷⁾. However, the pathogenicity of these species other than *Pseudomonas aeruginosa* in clinical development of UTI has still many unclear points to be elucidated yet, and it has not been experimentally analyzed yet also. In this experiment, we investigated the virulence of *Acinetobacter calcoaceticus*, *Pseudomonas cepacia*, and *Pseudomonas maltophilia* was tested in experimental UTI with mice. The relation between the UTI virulence of the organisms and their biological characteristics such as bacterial adhesion to the epithelial cell surfaces of the bladder and hemagglutination pattern was investigated. Moreover, the change of virulence was studied in compromised hosts treated with immunosuppressive drugs.

Materials and Methods

Animals

Five-week-old female mice of an outbred ddY strain weighing 18 to 20 gm (Shizuoka Agricultural Cooperative Association for Laboratory Animals, Hamamatsu, Japan) were used.

Bacterial strains

The following seven species of clinical isolates were used: *Acinetobacter calcoaceticus* subsp. *anitratus* five strains, *Pseudomonas cepacia* five strains, *Pseudomonas maltophilia* five strains, *Pseudomonas aeruginosa* four strains, *Escherichia coli* three strains, *Proteus mirabilis* two strains, and *Serratia marcescens* one strain. The test strains were cultured in nutrient broth (Nissui) at 37°C for 18 hours. Overnight cultures were harvested

by centrifugation, and washed twice in 0.1 M phosphate buffered saline (PBS, pH 7.2) and diluted for *in vitro* and *in vivo* studies.

Experimental intraperitoneal infection

Serial tenfold dilutions were prepared from the overnight culture and 0.5 ml each of dilutions was challenged intraperitoneally to eight mice per group, concurrently with 3% hog gastric mucin solution (Orthana Kemisk Fabrik A/S). The mice were examined for survival for a seven-day period, and LD₅₀ value (cells/mouse) was estimated by the Probit method.

Experimental urinary tract infection

Ascending urinary tract infection was induced by transurethral inoculation of a bacterial suspension⁸⁾. In brief, after 15-hour stoppage of water supply, mice were forced to void urine by gentle compression of the bladder via the external abdominal wall. Then anesthesia was carried out intraperitoneally with 50 mg/kg of sodium pentobarbital (Nembutal; Abott Laboratories, Co Ltd.). Then 0.05 ml of bacterial suspension containing about 10⁴ to 10⁷ cells was inoculated into the bladder via the urethra after disinfecting the circumference of urinary meatus with alcohol. Then the meatus was clipped for four hours to prevent the suspension from leaking. At specific intervals of time after inoculation, five to seven mice per group were bled to death and their bilateral kidneys were removed aseptically and homogenized in saline. Then the dilutions were plated for colony counts.

Hemagglutination test

Erythrocyte specimens from man, guinea pigs, and mice were suspended in Alsevers solution and kept at 4°C. Hemagglutination test was carried out by the Kerhonen method⁹⁾. In brief, the erythrocytes were washed with PBS and 3% erythrocytes PBS suspension was prepared and was mixed on a glass slide with 20 μ l each of bacterial suspension either in the presence or absence of 2% D-mannose. Agglutination was examined after ten minutes at 4°C.

Adhesion to epithelial cells of mouse bladder

Adhesion to the epithelial cells of the mouse bladder was determined by the method of Svanborg-Eden et al.¹⁰⁾. Epithelial cells from the mouse bladder were suspended in PBS at size of 10⁵ cells/ml. To this suspension was added PBS with 10⁸ bacterial cells/ml. After incubation at 37°C for 60 minutes, unattached bacteria were eliminated by repeated washing and stained with Giemsa. The number of bacteria attached to the epithelial cells was counted by light microscopy. Adhesion was defined as the mean number of bacteria attached to 100 epithelial cells.

Results

Experimental urinary tract infection in normal mice

The results of viable cell counts obtained from the kidneys at 48 hours after transurethral inoculation in normal mice are shown in Table 1. In case 10⁶ cells each of *A. calcoaceticus*, *P. cepacia*, and *P. maltophilia* were inoculated, the viable cell counts found per kidney ranged from 10^{3.7} to 10^{6.0}, 10^{3.7} to 10^{6.2}, and 10^{2.5} to 10^{4.3} cells, respectively. With an inoculum size of 10⁷ cells of the same species, the viable counts ranged from 10^{5.3} to 10^{7.8}, 10^{5.9} to 10^{6.0}, and 10^{5.9} to 10^{6.0} cells, respectively. Thus the incidence of bacterial recovery from the kidney and the degree of renal tissue disturbance (abscess formation) were found to be relatively low with these organisms. Only *A. calcoaceticus* Ac-54 showed a high renal recovery rate and a high tissue disturbance. On the other hand, with an inoculum size of 10⁴ cells/mouse, *E. coli*, *P. mirabilis*, *S. marcescens*, and *P. aeruginosa* showed the viable cell counts in the kidney ranging from 10^{6.2} to 10^{7.0}, 10^{7.4} to 10^{7.9}, 10^{6.7}, and 10^{7.1} to 10^{7.4} cells, respectively. These organisms showed a high tissue disturbance. These results suggest that the virulence of *A. calcoaceticus*, *P. cepacia*, and *P. maltophilia* in urinary tract infection was relatively mild.

Furthermore, the relation between the virulence in peritoneal infection (LD₅₀ values) and that in urinary tract infection was studied, and the results are presented in Fig. 1. In *A. calcoaceticus*, *P. cepacia*, and *P.*

Table 1. Bacterial populations in the kidneys of mice following challenge of various organisms

Organism		Log of viable counts/kidneys			
		10 ⁴ cells/mouse*	10 ⁵ cells/mouse	10 ⁶ cells/mouse	10 ⁷ cells/mouse
<i>A. calcoaceticus</i>	Ac-54	N.D.	N.D.	6.07±0.93 (3/7)**	7.76±0.82 (4/7)
	Ac-78	N.D.	N.D.	3.69±2.08 (0/7)	5.30±1.16 (0/7)
	Ac-126	N.D.	N.D.	4.69±1.72 (0/7)	5.96±1.63 (1/7)
	Ac-156	N.D.	N.D.	4.27±1.19 (0/7)	6.42±1.16 (2/7)
	Ac-164	N.D.	N.D.	4.43±1.93 (0/7)	5.64±1.92 (1/7)
<i>P. cepacia</i>	M-500	N.D.	N.D.	5.14±1.87 (1/7)	N.D.
	M-501	N.D.	N.D.	5.16±0.90 (0/7)	N.D.
	M-509	N.D.	N.D.	4.77±2.23 (0/7)	5.92±1.01 (1/7)
	M-511	N.D.	N.D.	5.01±1.43 (0/7)	N.D.
	M-527	N.D.	N.D.	3.69±1.89 (0/7)	5.96±1.51 (1/7)
<i>P. maltophilia</i>	M-601	N.D.	N.D.	4.27±1.96 (0/7)	N.D.
	M-603	N.D.	N.D.	3.00±1.76 (0/7)	N.D.
	M-605	N.D.	N.D.	3.36±1.38 (0/7)	6.00±1.51 (1/7)
	M-607	N.D.	N.D.	4.27±1.05 (0/7)	N.D.
	M-609	N.D.	N.D.	2.51±1.02 (0/7)	5.94±1.45 (1/7)
<i>E. coli</i>	KC-14	6.97±0.90 (5/7)	7.28±0.85 (7/7)	N.D.	N.D.
	No. 29	6.23±1.38 (4/7)	6.95±0.51 (6/7)	N.D.	N.D.
	ST0198	7.00±1.21 (7/7)	7.52±0.59 (7/7)	N.D.	N.D.
<i>P. mirabilis</i>	S-434	7.94±0.52 (7/7)	8.34±0.40 (7/7)	N.D.	N.D.
	F-181	7.37±0.77 (7/7)	8.11±0.35 (7/7)	N.D.	N.D.
<i>S. marcescens</i>	T-55	6.71±0.97 (5/7)	6.98±0.79 (7/7)	N.D.	N.D.
<i>P. aeruginosa</i>	E-2	7.19±0.68 (7/7)	7.92±0.58 (7/7)	N.D.	N.D.
	IFO3080	7.10±0.96 (7/7)	7.85±0.31 (7/7)	N.D.	N.D.
	IFO3445	7.31±0.77 (6/7)	7.98±0.69 (7/7)	N.D.	N.D.
	NCTC10490	7.40±0.67 (7/7)	7.90±0.59 (7/7)	N.D.	N.D.

* Inoculum size

** No. of mice with lesion/No. of tested mice

maltophilia except for *A. calcoaceticus* Ac-54 a relatively close relation between the two parameters was noted. Thus, the strains which were less lethal in peritoneal infection were demonstrated to show a lower recovery rate from the kidneys as well.

Virulence in urinary tract infection in compromised mice

Prednisolone, betamethasone (Shionogi Pharmaceutical & Co Ltd.), and lysozyme (Eisai Co Ltd.) were used as anti-inflammatory drugs. 0.08 mg of prednisolone and 0.4 mg of betamethasone were administered orally and 0.2 mg of lysozyme was intramuscularly to mice as a single daily dose for seven days. At Day 8, the following day after the final treatment, the mice were transurethrally infected, and the viable cell counts in the kidney were counted at 48 hours after inoculation. The results are shown in Table 2. The pre-treatment with either prednisolone or betamethasone slightly enhanced the susceptibility to renal infection with all the strains tested. In the case of lysozyme, however, little difference in the number of organisms was noted between the treated and the control mice.

As immunosuppressive drugs, cyclophosphamide (Shionogi Pharmaceutical & Co Ltd.) and azathiopurine (Tanabe Pharmaceutical Co Ltd.) were used. 4 mg of cyclophosphamide was injected intraperitoneally to mice and at four days after treatment, bacterial suspension were inoculated. Azathiopurine was administered orally at a daily dose of 1 mg for seven days, and at Day 8, the following day after final treatment, bacterial suspensions were inoculated into mice. At 48 hours after inoculation, viable cell counts in the kidney were

Fig. 1. Relation between LD₅₀ in mice with peritoneal infection and renal recovery of organisms in urinary tract infection

Table 2. Effect of prednisolone, betamethasone, and lysozyme treatment on pathogenicity of glucose non-fermentative rods in the mouse kidneys

Organism	Inflammatory drug	Log of viable counts/kidneys	
		Non-treated	Treated
<i>A. calcoaceticus</i> Ac-78	Prednisolone	3.25±1.45 (0/5)*	5.00±1.30 (1/5)
<i>A. calcoaceticus</i> Ac-126		3.68±1.80 (0/5)	4.78±1.71 (1/5)
<i>A. calcoaceticus</i> Ac-156		3.43±1.42 (0/5)	4.80±1.71 (0/5)
<i>A. calcoaceticus</i> Ac-164		2.85±1.00 (0/5)	4.50±1.30 (0/5)
<i>P. cepacia</i> M-527		4.20±1.68 (0/5)	5.60±1.21 (3/5)
<i>P. maltophilia</i> M-609		4.80±0.78 (0/5)	5.00±1.71 (2/5)
<i>A. calcoaceticus</i> Ac-78	Betamethasone	4.10±1.91 (0/5)	6.21±0.50 (3/5)
<i>A. calcoaceticus</i> Ac-126		4.80±0.65 (0/5)	5.71±1.21 (2/5)
<i>A. calcoaceticus</i> Ac-156		4.78±0.71 (0/5)	5.70±0.60 (1/5)
<i>A. calcoaceticus</i> Ac-164		5.00±1.21 (1/5)	4.95±1.80 (1/5)
<i>P. cepacia</i> M-527		4.21±1.80 (1/5)	6.80±0.30 (3/5)
<i>P. maltophilia</i> M-609		5.00±1.38 (1/5)	5.85±1.37 (1/5)
<i>A. calcoaceticus</i> A -78	Lysozyme	3.30±2.00 (0/5)	4.00±1.78 (0/5)
<i>A. calcoaceticus</i> Ac-126		3.40±1.85 (0/5)	4.70±1.28 (0/5)
<i>A. calcoaceticus</i> Ac-156		3.20±1.55 (0/5)	3.20±1.75 (0/5)
<i>A. calcoaceticus</i> Ac-164		2.30±1.21 (0/5)	3.40±1.50 (0/5)
<i>P. cepacia</i> M-527		4.20±1.65 (0/5)	4.50±1.70 (1/5)
<i>P. maltophilia</i> M-609		4.50±1.00 (0/5)	3.00±0.65 (0/5)

* No. of mice with lesion/No. of tested mice

Mice were inoculated with $7-9 \times 10^5$ cells for prednisolone assay, $1-3 \times 10^6$ cells for betamethasone assay, and $6-9 \times 10^5$ cells for lysozyme assay.

counted, as Table 3. In cyclophosphamide treatment, the bacterial recovery from the kidney was about 100 to 1,000 times higher in the treated than in the non-treated mice, showing a trend of higher susceptibility to *A. calcoaceticus* and *P. cepacia* was apparently higher than those of the control mice. With *P. maltophilia*, however, little difference was noted between the treated and the non-treated mice.

Furthermore, the virulence was studied in experimentally induced diabetic mice. 2.5mg of streptozotocin (Sigma Chemical Co.) was injected intraperitoneally into mice and at Day 10 bacterial suspensions

Table 3. Effect of cyclophosphamide and azathiopurine treatment on pathogenicity of glucose non-fermentative rods in the mouse kidneys

Organism		Log of viable counts/kidneys			
		Cyclophosphamide		Azathiopurine	
		Non-treated	Treated	Non-treated	Treated
<i>A. calcoaceticus</i>	Ac-78	3.10±1.40 (0/5)*	6.00±1.55 (3/5)	4.10±1.80 (0/5)	6.20±0.30 (2/5)
<i>A. calcoaceticus</i>	Ac-126	3.90±1.75 (1/5)	6.23±1.41 (4/5)	4.65±1.75 (0/5)	6.02±1.30 (4/5)
<i>A. calcoaceticus</i>	Ac-156	3.72±0.95 (0/5)	5.50±1.98 (2/5)	4.70±0.90 (0/5)	6.00±1.28 (2/5)
<i>A. calcoaceticus</i>	Ac-164	3.95±1.81 (0/5)	5.75±0.40 (1/5)	4.50±1.95 (1/5)	6.80±0.95 (3/5)
<i>P. cepacia</i>	M-527	3.00±1.22 (0/5)	5.70±0.25 (0/5)	4.00±1.78 (1/5)	6.80±1.10 (4/5)
<i>P. maltophilia</i>	M-609	3.00±1.10 (0/5)	5.00±1.80 (1/5)	4.85±1.81 (1/5)	5.10±2.10 (2/5)

* No. of mice with lesion/No. of tested mice

Mice were inoculated with $5-7 \times 10^5$ cells for cyclophosphamide assay and $1-4 \times 10^6$ cells for azathiopurine assay.

Table 4. Effect of streptozotocin treatment on pathogenicity of glucose non-fermentative rods in the mouse kidneys

Organism		Log of viable counts/kidneys	
		Non-treated	Treated
<i>A. calcoaceticus</i>	Ac-78	4.10±1.95(1/7)*	5.00±1.54(3/7)
<i>A. calcoaceticus</i>	Ac-126	3.95±1.63(0/7)	4.85±1.73(1/7)
<i>A. calcoaceticus</i>	Ac-156	3.10±1.10(0/7)	5.00±2.53(3/7)
<i>A. calcoaceticus</i>	Ac-164	4.00±0.95(0/7)	4.50±1.78(1/7)
<i>P. cepacia</i>	M-527	4.50±1.35(0/7)	4.30±2.10(2/7)
<i>P. maltophilia</i>	M-609	3.23±1.32(0/7)	4.20±2.51(2/7)

* No. of mice with lesion/No. of tested mice

Mice were inoculated with $0.8-2 \times 10^6$ cells.

were inoculated. The mean blood sugar level at Day 10 was 160 mg/dl in the streptozotocin-treated mice and 72 mg/dl in normal mice. At 48 hours after inoculation, viable cell counts in the kidneys were counted, and the results are summarized in Table 4. The pre-treatment with streptozotocin showed only a minimal change in susceptibility to *P. cepacia* and *P. maltophilia*. The susceptibility to *A. calcoaceticus*, however, was about 10 to 100 times higher than that of the control mice.

Hemagglutination test

The capacity to agglutinate erythrocytes of man, guinea pigs, and mice was studied in glucose non-fermentative rods, as shown in Table 5. Most strains having agglutinated the erythrocytes of man and guinea pigs showed an inhibitory reaction against agglutination with the addition of mannose. These organisms were lacking in the capacity for agglutinating mouse erythrocytes.

Adhesion to epithelial cells of mouse bladder

The *in vitro* study on the ability of glucose non-fermentative rods to adhere to the epithelial cells of mouse bladder are shown in Table 5. *A. calcoaceticus* Ac-54, which was highly virulent was also found to have a high adhesive capacity to epithelial cells, but the other strains were shown to be less adhesive. Accordingly, any clear relationship between hemagglutination and adhesive activity was not observed.

Discussion

In recent years, various infectious diseases caused by glucose non-fermentative rods except *P. aeruginosa* have come to be described. However, there is still many unclear points on the pathogenicity of these strains.

Table 5. Relation between hemagglutination of glucose non-fermentative rods and their attachment to epithelial cells of mouse bladder

Organism		Erythrocyte agglutinated			Mean adhesion
		Human	Guinea pig	Mouse	
<i>A. calcoaceticus</i>	Ac-54	MS	MS	—	32
<i>A. calcoaceticus</i>	Ac-78	—	MS	—	15
<i>A. calcoaceticus</i>	Ac-126	—	—	—	8
<i>A. calcoaceticus</i>	Ac-156	MS	MS	—	17
<i>A. calcoaceticus</i>	Ac-164	—	MS	—	9
<i>P. cepacia</i>	M-500	MS	MS	—	14
<i>P. cepacia</i>	M-501	MS	MS	—	13
<i>P. cepacia</i>	M-509	—	—	—	11
<i>P. cepacia</i>	M-511	—	—	—	7
<i>P. cepacia</i>	M-527	—	—	—	9
<i>P. maltophilia</i>	M-601	—	—	—	8
<i>P. maltophilia</i>	M-603	MS	MS	—	14
<i>P. maltophilia</i>	M-605	—	—	—	7
<i>P. maltophilia</i>	M-607	—	MS	—	11
<i>P. maltophilia</i>	M-609	—	—	—	12
<i>E. coli</i>	KC-14	MS	MS	—	37
<i>P. aeruginosa</i>	E-2	MS	MS	—	44
<i>P. aeruginosa</i>	NCTC10490	MS	MS	—	34

MS : mannose-sensitive

— : no agglutination

In our previous papers, we described that *Acinetobacter* was pathogenic to experimental mouse infection in spite of its low virulence⁸⁾¹¹⁾. This suggests the possibility that the organisms of low virulence such as *Acinetobacter* may induce infectious diseases in the presence of diminished host defense mechanisms such as caused by underlying diseases or immunosuppressive therapy. In the present experiments, therefore, we carried out the basic study on the virulence of glucose non-fermentative rods such as *A. calcoaceticus*, *P. cepacia*, and *P. maltophilia* in urinary tract infections.

In general, the virulence of these organisms in urinary tract infections was demonstrated to be relatively mild. A clear relation between the virulence in peritoneal infection and that in urinary tract infection was noted. Namely, when a strain was less virulent in urinary tract infection, it was likewise less virulent in peritoneal infection. However, Nishi et al.¹²⁾ reported that the virulence factors of *P. aeruginosa* in UTI may be different from those in peritoneal infection. These relations should be further in the future.

Recently, anti-inflammatory drugs are generally used in all clinical fields for the treatment of inflammation in order to inhibit inflammatory reactions of the living body. In the present experiments, we investigated the effect of three anti-inflammatory drugs on the infections with glucose non-fermentative organisms in mice. The mice treated with either betamethasone or prednisolone were susceptible to those organisms, but little effect was noted on the infection in the mice treated with lysozyme. However it cannot be concluded that under lysozyme treatment, susceptibility to these organisms can be prevented. The method of administration should be studied further in the future. Moreover, immunosuppressive drugs are known as the drugs affecting the bacterial susceptibility of the patient. Therefore, the effect of these drugs on the pathogenicity of these organisms was studied in mice. The mice given cyclophosphamide or azathiopurine showed more susceptibility to these organisms than the non-treated ones. Therefore, immunosuppressive agents should be given with a great caution.

From old times, diabetes mellitus is known as one of the underlying diseases to reduce the function of host-defense mechanism against diseases. Therefore, the susceptibility to these organisms was studied in the streptozotocin-induced diabetic mice. These mice were more susceptible against *Acinetobacter* than the non-treated ones, but no effect was observed with *P. cepacia* and *P. maltophilia*. However, this cannot be concluded as the evidence that the susceptibility to *P. cepacia* and *P. maltophilia* does not change even in the presence of diabetes. Further careful studies should be carried out regarding the virulence in diabetic mice. From the these results, it has been proven that immunosuppression or diabetes is generally the factor for precipitating the infections with glucose non-fermentative rods.

Attachment of bacteria to the mucosal surfaces of a susceptible host is now recognized as an important step to bacterial colonization and onset of infection. The ability of bacteria to adhere to the epithelial cells *in vitro* appears to be dependent on the surface components of both host and bacterial cells. Bacterial adhesion is classified according to the agglutination patterns which manifest when bacteria bind to the erythrocytes of various species of animals.

In the present experiment, we investigated the relation between hemagglutination and the capacity of bacterial attachment to epithelial cells of mouse bladder. All the organisms except *A. calcoaceticus* Ac-54 were shown to have low adhesion. Furthermore, the hemagglutination patterns were mannose-sensitive to human and guinea pig erythrocytes. These results indicate that while the glucose non-fermentative rods tested were certainly pathogenic in urinary tract infection of mice, their pathogenicity was extremely low.

Although it may be risky attempt to apply all these results to human, these organisms are presumed to be of low virulence to humans as well. Unlike experimental infections with animals, however, the infectious disease caused by even the low virulent organisms such as *A. calcoaceticus*, *P. cepacia*, and *P. maltophilia* are liable to occur under abnormal physiological condition of the subject and therefore through cautions should be given to the treatment in clinical practice.

Reference

- 1) Shimada, K.: Opportunistic infection. *Farumashia*, 16, 745—749, 1980.
- 2) Saito, A. and Ihara, H.: Opportunistic infection. *The Igaku no Ayumi*, 111, 976—981, 1979.
- 3) Alami, S.Y. and Riley, Jr. H.D.: Infections caused by *Mimae*, with special reference to *Mima polymorpha* a review. *Amer. J. Med. Sci.*, 252, 537—544, 1966.
- 4) Kozub, W.R., Bucolo, S., Sami, A.W., Chatman, C.E. and Pribor, H.C.: Gonorrhea-like urethritis due to *Mima polymorpha* var. *oxidans*. *Arch. Int. Med.*, 122, 514—516, 1968.
- 5) Pedersen, M.M., Marso, E. and Pickett, M.J.: Nonfermentative bacilli associated with man: III. Pathogenicity and antibiotic susceptibility. *Amer. J. Clin. Path.*, 54, 178—192, 1970.
- 6) Wands, J.R., Mann, R.B., Jackson, D. and Butler, T.: Fatal community-acquired *Herella* pneumonia in chronic renal disease. *Amer. Rev. Resp. Dis.*, 108, 964—967, 1973.
- 7) Richardson, R.I.: *Mimeae* septicemia. *J. Amer. Med. Assoc.*, 207, 1716—1717, 1969.
- 8) Obana, Y., Orikasa, Y., Nishino, T. and Tanino, T.: Studies on *Acinetobacter calcoaceticus*. IV: Experimental urinary tract infections in mice. *Chemotherapy* 30, 996—1003, 1982.
- 9) Korhonen, T.K.: Yeast cell agglutination by purified enterobacteria pilli. *FEMS Microbiol. Lett.*, 6, 421—425, 1979.
- 10) Hagberg, L., Jdal, U., Korhonen, T.K., Lidin-Janson, G., Lindberg, U. and Svanbory Eden, C.: Adhesion, hemagglutination, and virulence of *Escherichia coli* causing urinary tract infections. *Infect. immun.*, 31, 564—570, 1981.
- 11) Obana, Y., Nishino, T. and Tanino, T.: Studies on *Acinetobacter calcoaceticus*. The virulence and the therapeutic efficacy of antibiotics in mice. *J.J.A. Inf. D.*, 56, 753—761, 1982.
- 12) Nishi, T. and Tsuchiya, K.: Experimental urinary tract infection with *Pseudomonas aeruginosa* in mice. *Infect. Immun.*, 22, 508—515, 1978.

マウス実験的腎盂腎炎に於けるブドウ糖非発酵菌の起病性について

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臨床分離 *Acinetobacter calcoaceticus*, *Pseudomonas cepacia* および *Pseudomonas maltophilia* の尿路感染性について、マウスを用いて検討を行った。

全般的に、これらの菌種の正常マウスに対する尿路感染性は低いことが認められた。またこれらの菌種の起病性に及ぼす抗炎症剤、免疫抑制剤の

影響について検討したところ、betamethasone, prednisolone, cyclophosphamide および azathiopurine 前投与マウスの感染性は無投与群よりも上昇することが認められた。

マウス膀胱上皮細胞への付着性について検討したところ、付着性は比較的低かった。さらにこれらの菌種の一部は、ヒトおよびモルモットの赤血球を凝集する性質を有していたが、mannose の添加により阻害された。

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