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AN OBSERVATION ON ANTIBACTERIAL ACTIVITY OF GENTAMICIN AGAINST MAIN ORGANISMS ISOLATED CLINICALLY: (I) GENTAMICIN SENSITIVITY OF BACTERIA

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antibacterial drug; chemotherapy; gentamicin; clinical bacteriology

Minoru KOBAYASHI, M.D., Hisao TAKAMI and Nobumasa KATAOKA, M. Agr. *An Observation on Antibacterial Activity of Gentamicin against Main Organisms Isolated Clinically: (1) Gentamicin Sensitivity of Bacteria:* Kobe J. Med. Sci. 20, 103-118, December 1974——Gentamicin (abbreviated hereinafter to GM) has been reported to have a potent antimicrobial activity against gram-negatives, especially *E. coli*, *Klebsiella*, *Pseudomonas* and *Proteus*. We examined gentamicin sensitivity of organisms isolated in our laboratories during one year from September 1972 to August 1973.

One thousand five hundred and ninety-nine strains of gram-positives and 2,960 strains of gram-negatives were selected, and the disk method was applied throughout the study. Among them 272 strains were randomly selected for measuring MIC (minimal inhibitory concentration).

The data of the study revealed that: the gram-positives displayed high sensitivity to GM (the incidence of sensitivity was as high as 82.0 per cent for all the strains tested) except for *Streptococcus faecalis*, and in most cases, a significantly higher sensitivity than to other chemotherapeutic agents.

Ninety-two per cent of all the strains were represented by *E. coli*, *Pseudomonas*, *Klebsiella*, *Enterobacter* and *Proteus*. These gram-negatives were all highly sensitive, and significantly more sensitive than to CL (Colistin), KM (Kanamycin) or AB-PC (Ampicillin). Moreover, gentamicin is superior to the other chemotherapeutic agents tested in respect to the range of MIC in all but a few exceptional cases.

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INTRODUCTION

Gentamicin (GM) has been proved to have an excellent antimicrobial activity against gram-negative bacilli of low virulence and of high incidence such as *E. coli*, *Proteus*, *Aeromonas*, *Pseudomonas*, etc. The drug has also been used in large quantities in daily practice for treatment of various kinds of infection.

This report summarized the data of our observations made since September 1972 on the antimicrobial activity of GM against clinically isolated organisms. Sensitivity tests using GM-disk were done as routine techniques. MIC was measured using organisms randomly selected from the test strains.

MATERIALS AND METHODS

(1) *Organisms used for test*

One thousand five hundred and ninety-nine strains of gram-positive organisms and 2,960 strains of gram-negative organisms which were isolated in our laboratories during one year from September 1972 to August 1973, were selected. Two hundred and seventy-two strains of organisms from other sources were additionally used. The test organisms are listed in Table 1. Among them, 272 strains were randomly selected for measuring MIC (refer to Table 2).

Table 1 Organisms tested.

Organisms	No. of strain
Gram-positive	
Staphylococcus aureus	307
Staphylococcus epidermidis	485
Streptococcus viridans	224
Streptococcus feacalis	419
Corynebacterium diphtheroides	46
Streptoccus hemolyticus (A-group)	47
Peptostreptococcus	25
Anaerobic corynebacterium	7
Clostridium perfringens	9
Peptococcus	5
Diplococcus pneumoniae	18
Actinomyces	2
Catenabacterium	5
Total	1,599

(to continue!)

Gram-negative	
E. coli	1,114
Klebsiella	564
Proteus mirabilis	157
Proteus vulgaris	25
Rettgerella	25
Providencia	13
Pseudomonas	594
Citrobacter	58
Enterobacter	166
Morganella	129
Hafnia	24
Alkaligenes faecalis	42
Acinetobacter	19
Flavobacterium	6
Bacteroides	9
Fusobacter um	5
Hemophilus sp.	4
Achromobacter	6
Total	2,960

Table 2 Number of strains tested for MIC.

Organisms	No. of strain
Gram-positive	
Staph. aureus	10
Staph. epidermidis	24
Diplo. pneumoniae	2
Str. faecalis	4
Subtotal	40
Gram-negative	
E. coli	44
Klebsiella	60
Enterobacter	34
Morganella	6
Pseudomonas	64
Acinetobacter	4
Flavobacterium	2
Prot. mirabilis	
Citrobacter	6
Prot. vulgaris	4
Subtotal	232
Total	272

(2) *Sensitivity test*

The sensitivity to GM was measured, in comparison with that to Kanamycin (abbreviated to KM) in the case of gram-positive organisms and those to KM, Colistin (abbreviated to CL) and Ampicillin (abbreviated to AB-PC) in the case of gram-negative organisms. "One concentration disk" (Showa Pharmaceutical Co., Japan) was used throughout the study and the drugs in doses as indicated in Table 3 were used for estimation of MIC.

The disk method was applied by mixed dilution as described in literature. The MIC was determined according to the procedures set forth by the Japanese Association of Chemotherapeutics.

Table 3 Drugs and doses used for estimation of MIC.

Drug	Doses
Gentamicin sulfate	578 mcg/mg
Kanamycin sulfate	1,000 mcg/mg
Colis in sulfate	19,620 u/mg
Ampici lin	1,000 mcg/mg

For the disk method, the judgements were based on two criteria: "sensitive" or category (卅) or (艹) and "insensitive" or category (+) or (−). MIC was graphically shown in 16 scales up to 400 mcg/ml and over 400 mcg/ml using double dilution from 0.02 mcg/ml onwards.

RESULTS

Judgements of sensitivity.

Sensitivity	Category
Sensitive	卅
	艹
Insensitive	+
	−

Overall figures of the disk sensitivity are summarized in Table 4 and the data classified by the test specimens are shown in Tables 5 to 11.

Isolates from the urine were of the highest incidence, accounting for 43.6% for gram-positives and 75.7% for gram-negatives. The other isolates were from the sputum, pus, secretes, puncture fluid, mucus of the throat, and others.

Table 4 Drug sensitivity of organisms isolated from clinical specimens.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	307	307(100.0)*	292(95.1)		
Staph. epidermidis	485	480(99.0)	429(88.5)		
Str. viridans	224	202(90.2)	80(30.7)		
Str. faecalis	419	203(48.3)	103(24.6)		
Cory. diphtheroides	46	35(76.1)	25(54.3)		
Catenabacterium	5	5(100.0)	4(80.0)		
Str. hemolyticus	47	39(83.0)	22(46.8)		
Anaerobic corynebact.	7	6(85.7)	4(57.1)		
Peptococcus	5	1(20.0)	0		
Peptostreptococcus	25	22(88.0)	9(36.0)		
Clost. perfringens	9	0	0		
Diplo. pneumonia	18	9(50.0)	1 (5.6)		
Actinomyces	2	2(100.0)	0		
Total	1,599	1,311(82.0)	969(60.9)		
Gram-negative					
E. coli	1,114	1,111(99.7)	912(81.9)	1,105(99.2)	784(70.4)
Klebsiella	564	560(99.3)	359(63.7)	556(98.6)	137(24.3)
Prot. mirabilis	157	156(99.4)	157(100.)	4(2.5)	133(84.7)
Prot. vulgaris	25	25(100.)	22(88.0)	1(4.0)	10(40.0)
Rettgerella	25	20(80.0)	21(84.0)	5(20.0)	19(76.0)
Providensia	13	12(92.3)	8(61.5)	1(7.7)	5(38.5)
Pseudomonas	594	566(95.3)	194(32.7)	589(99.2)	31(5.2)
Citrobacter	58	57(98.3)	41(70.7)	56(96.6)	31 (53.5)
Enterobacter	166	165(99.4)	90(54.2)	165(99.4)	75(45.2)
Morganella	129	117(90.7)	21(16.3)	33(25.6)	6(4.7)
Hafnia	24	24(100.)	19(79.2)	22(91.7)	8(33.3)
Alkaligenes	42	40(95.2)	33(78.6)	32(76.2)	10(23.8)
Acinetobacter	19	19(100.)	12(63.2)	16(84.2)	9(47.4)
Flavobacterium	6	1(16.7)	0	0	0
Bacteroides	9	1(11.1)	0	0	0
Fusobacterium	5	5(100.)	0	4(80.0)	5(100.)
Hemophilis	6	6(100.)	5(83.3)	6(100.)	1(16.7)
Achromobacter	4	4(100.)	3(75.0)	4(100.)	4(100.)
Total	2,960	2,899(97.6)	1,897(64.1)	2,599(87.8)	1,255(42.4)

*Parenthesis indicates percentage of strains belonging to each category.
This legend will be applied in latter tables

Table 5 Drug sensitivity of organisms isolated from the urine.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph.aureus	20	20(100)	20(100)		
Staph.epidermidis	200	196(98.0)	176(88.0)		
Str. viridans	100	92(92.0)	44(44.0)		
Str. faecalis	344	184(53.5)	84(24.4)		
Cory. diphtheroides	25	15(60.0)	16(64.0)		
Catenabacterium	5	5(100)	4(80.0)		
Str. hemolyticus	3	3(100)	0		
Total	697	515(73.9)	344(49.3)		
Gram-negative					
E. coli	948	948(100)	816(86.1)	944(99.5)	644(67.9)
Klebsiella	392	392(100)	240(61.2)	388(99.0)	84(21.4)
Prot. mirabilis	134	134(100)	134(100)	2(1.5)	115(85.5)
Prot. vulgaris	20	20(100)	17(85.0)	0	5(25.0)
Rettgerella	20	19(95.0)	17(85.0)	5(25.0)	18(90.0)
Providensia	5	4(80.0)	0	1(20.0)	0
Pseudomonas	392	380(97.0)	116(29.5)	392(100)	5(1.3)
Citrobacter	44	44(100)	28(63.6)	43(97.7)	12(27.3)
Enterobacter	104	104(100)	28(26.9)	104(100)	20(19.2)
Morganella	112	112(100)	100(89.2)	8(7.2)	32(28.6)
Hafnia	16	16(100)	12(75.0)	15(93.7)	4(25.0)
Alkaligenes faecalis	42	40(95.2)	33(78.6)	32(76.2)	10(23.8)
Acinetobacter	4	4(100)	0	4(100)	0
Flavobacterium	6	1(16.7)	0	0	0
Total	2,239	2,218(99.1)	1,541(68.8)	1,938(86.6)	949(42.2)

Table 6 Drug sensitivity of organisms isolated from the pus.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive	124	124(100)	113(91.1)		
Staph. aureus					
Staph. epidermidis	129	128(99.2)	109(84.5)		
Str. viridans	57	53(93.0)	13(22.8)		
Str. faecal s	45	9(20.0)	4(8.9)		
Cory. diphtheroides	9	8(88.9)	1(11.1)		
Anaerobic coryneb.	3	2(66.7)	0		
Str. hemolyticus	25	17(68.0)	9(36.0)		
Peptococcus	5	1(20.0)	0		
Peptostreptococcus	13	12(92.3)	1(7.7)		
Clost. perfringens	9	0	0		
Total	416	354(85.1)	250 (60.1)		
Gram-negative					
E. coli	58	57(91.3)	48(86.1)	56(82.2)	49(56.3)
Klebsiella	32	31(96.9)	31(96.9)	30(93.7)	9(28.1)
Prot. mirabilis	9	8(88.8)	9(100)	0	5(55.6)
Providens a	4	4(100)	4(100)	0	4(100)
Rettgerella	5	1(20.0)	4(80.0)	0	1(20.0)
Pseudomonas	45	44(97.7)	40(88.9)	44(97.9)	2(4.4)
Enterobacter	29	28(96.9)	29(100)	28(96.6)	29(100)
Morganella	4	4(100)	4(100)	0	1(25.0)
Hafnia	4	4(100)	4(100)	3(75.0)	0
Bacteroides	13	4(30.8)	4(30.8)	3(23.1)	12(92.3)
Fusobacterium	5	5(100)	0	4(80.0)	5(100)
Total	208	190(91.3)	177(85.1)	171(82.2)	117(56.3)

Table 7 Drug sensitivity of organisms isolated from the sputum.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	38	38(100)	38(100)		
Staph. epidermidis	5	5(100)	5(100)		
Diplo. pneumoniae	9	9(100)	1(11.1)		
Total	52	52(100)	44(84.6)		
Gram-negative					
E. coli	26	26(100)	26(100)	25(100)	26(100)
Klebsiella	90	89(98.9)	53(58.9)	88(97.8)	30(33.3)
Pseudomonas	89	84(91.4)	17(19.1)	88(98.9)	13(14.6)
Citrobacter	5	5(100)	5(100)	4(80.0)	1(20.0)
Enterobacter	24	24(100)	24(100)	24(100)	17(70.8)
Hafnia	4	4(100)	3(75.0)	4(100)	4(100)
Acinetobacter	13	13(100)	12(92.3)	12(92.3)	6(69.2)
Achromobacter	4	4(100)	3(75.0)	4(100)	4(100)
Total	255	249(97.6)	143(56.1)	294(97.6)	104(40.8)

Table 8 Drug sensitivity of organisms isolated from the secretes.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	72	72(100)	72(100)	69(95.8)	
Staph. epidermidis	84	84(100)	73(86.9)		
Str. viridans	44	38(86.3)	14(31.8)		
Str. faecalis	19	8(42.1)	9(47.4)		
Cory. diphtheroid.	9	9(100.)	5(55.6)		
Str. hemolyticus	4	4(100.)	1(25.0)		
Peptostreptococcus	5	4(80.0)	5(100.)		
Total	237	219(92.4)	176(74.3)		
Gram-negative					
E. coli	34	33(97.0)	29(85.3)	33(97.0)	26(76.5)
Klebsiella	22	21(95.5)	13(59.1)	22(100.)	2(9.1)
Prot. mirabilis	5	5(100.)	5(100.)	1(20.0)	4(80.0)
Providensia	4	4(100.)	4(100.)	0	1(25.0)
Psudomonas	49	41(83.7)	13(26.5)	48(98.0)	6(12.2)
Enterobacter	4	4(100.)	4(100.)	4(100.)	4(100.)
Morganella	13	13(100.)	9(69.2)	1(7.7)	5(38.5)
Hemophilus	6	6(100.)	5(83.3)	6(100.)	1(16.7)
Total	137	127(92.7)	82(59.9)	115(83.9)	49(35.8)

Table 9 Drug sensitivity of organisms isolated from the puncture fluid.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	13	13(100.)	13(100.)		
Staph. epidermidis	35	35(100.)	35(100.)		
Str. viridans	9	5(55.6)	6(55.6)		
Peptostreptococcus	7	6(85.7)	3(42.9)		
Total	64	51(92.2)	55(89.9)		
Gram-negative					
E. coli	18	18(100.)	18(100.)	18(100.)	18(100.)
Klebsiella	4	4(100.)	0	4(100.)	1(25.0)
Prot. mirabilis	9	9(100.)	9(100.)	1(11.1)	9(100.)
Prot. vulgaris	5	5(100.)	5(100.)	1(20.0)	5(100.0)
Total	36	36(100.)	32(88.9)	24(66.7)	33(91.7)

Table 10 Drug sensitivity of organisms isolated from the mucus of the throat.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	9	9(100.)	9(100.)		
Str. hemolyticus	15	15(100.)	12(80.0)		
Total	24	24(100.)	21(87.5)		
Gram-negative					
Kle bsiella	18	18(100.)	17(94.4)	18(100.)	10(55.6)
Pseudomonas	6	5(83.3)	1(16.7)	6(100.)	1(16.7)
Total	24	23(95.8)	18(75.0)	24(100.)	11(45.8)

Table 11 Drug sensitivity of organisms isolated from other specimens.

Organism	No. of strain tested	No. of strain sensitive to			
		GM	KM	CL	AB-PC
Gram-positive					
Staph. aureus	31	31(100.)	30(96.9)		
Staph. epidermidis	32	32(100.)	31(96.9)		
Str. viridans	14	14(100.)	5(35.7)		
Str. faecalis	11	2(18.2)	6(54.5)		
Cory. diphtheriodes	3	3(100.)	3(100.)		
Anaerobic corynebact.	4	4(100.)	4(100.)		
Actinomyces	2	2(100.)	0		
Total	97	88(90.7)	79(81.4)		
Gram-negative					
E. coli	30	29(96.7)	23(76.7)	30(100.)	21(70.0)
Klebsiella	6	5(83.3)	5(83.3)	6(100.)	1(16.7)
Pseudomonas	13	12(92.3)	7(53.8)	11(84.6)	4(30.8)
Citrobacter	9	8(88.9)	8(88.9)	9(100.)	2(22.2)
Enterobacter	5	5(100.)	5(100.)	5(100.)	5(100.)
Acinetobacter	2	2(100.)	0	0	0
Bacyeroides	3	0	0	0	3(100.)
Total	68	61(83.7)	48(70.5)	61(83.7)	36(52.9)

Seven hundred and eighty-seven out of 792 strains of *Staphylococcus* (99.4%) proved to be sensitive to GM; this incidence of sensitivity is higher than that of KM sensitivity (92.6%). The same statement can be made as to *Str. viridans* (GM 90.2%; KM 35.7%) and *Str. hemolyticus* (GM 83.0%; KM 46.2%). *Streptococcus faecalis* on the contrary, proved to be less sensitive to GM generally, although there existed a significant difference in its sensitivity to GM and KM; only 203 (48.4%) of 419 strains were found sensitive to GM. Among the gram-negative isolates, *E. coli* was of overwhelming incidence, accounting for 37.6% of the total. Next to this were *Pseudomonas* (20.1%), *Klebsiella* (19.1%), *Enterobacter* (5.6%), *Proteus mirabilis* (5.3%) and *Morganella* (4.4%). Altogether, these kinds of organisms account for 92.0% of the gram-negatives detected and 59.8% of the total isolates.

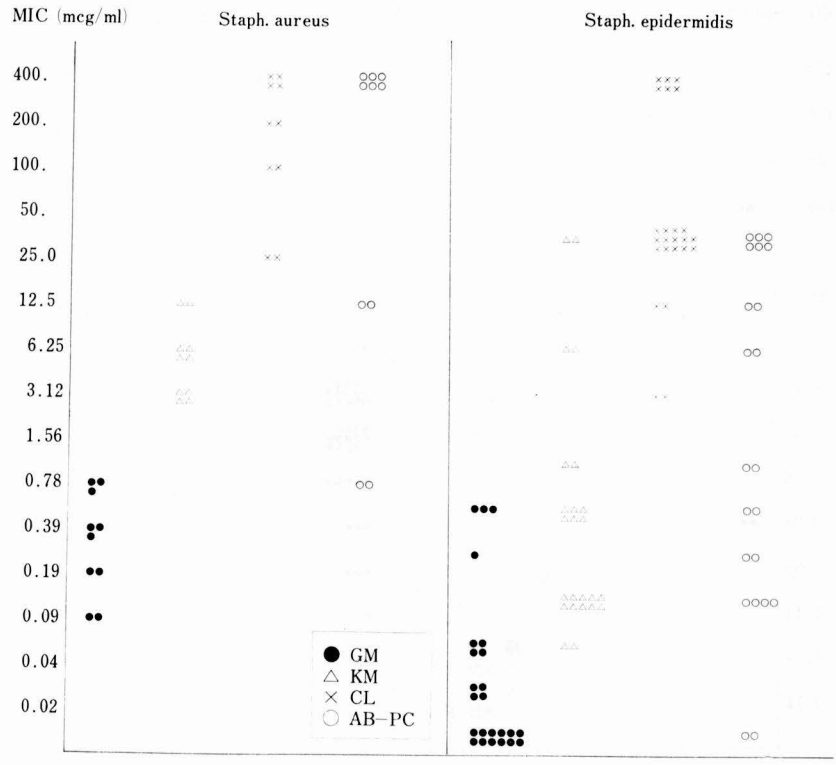
All of these gram-negative organisms proved highly sensitive to GM; incidence of sensitivity being 99.7% for *E. coli*, 99.3% for *Klebsiella*, 99.4% for *Proteus mirabilis*, 95.3% for *Pseudononas*, 99.4% for *Enterobacter* and 90.7% for *Morganella*. Such sensitivity figures were not only significantly different from that to KM or AB-PC simultaneously tested, but also slightly higher than that of CL, which usually displays a high antimicrobial activity against these organisms. As to the difference from CL, 330 (94.6%) of 349 strains of *Proteus-Providence* group

were more sensitive to GM as compared with only 44 strains (12.6%) that were sensitive to CL. The same applied to *Alkaligenes*, though limited in number of strains tested, as well as the strains studied as a whole. Of 272 strains randomly selected (as indicated in Table 2), MIC and disk sensitivity were examined in parallel. The results obtained are shown in Figs 1 to 4.

1) *Staphylococcus aureus*

As shown in Fig. 1, MIC for GM was distributed below 1.56 mcg/ml for all of 10 strains, showing a marked difference from that for CL or AB-PC. In the disk tests conducted simultaneously, all strains proved to be sensitive; there was certain discrepancy between the results of MIC and disk sensitivity.

Fig. 1 MIC ranges for *Staph. aureus* and *Staph. epidermidis*.



No. of strains sensitive or insensitive to test drugs (by disk method).

St. aureus	GM	KM	CL	AB-PC	St. epidermidis	GM	KM	CL	AB-PC
sensitive	10	10	10	10	sensitive	24	24	24	24
insensitive	0	0	0	0	insensitive	0	0	0	0

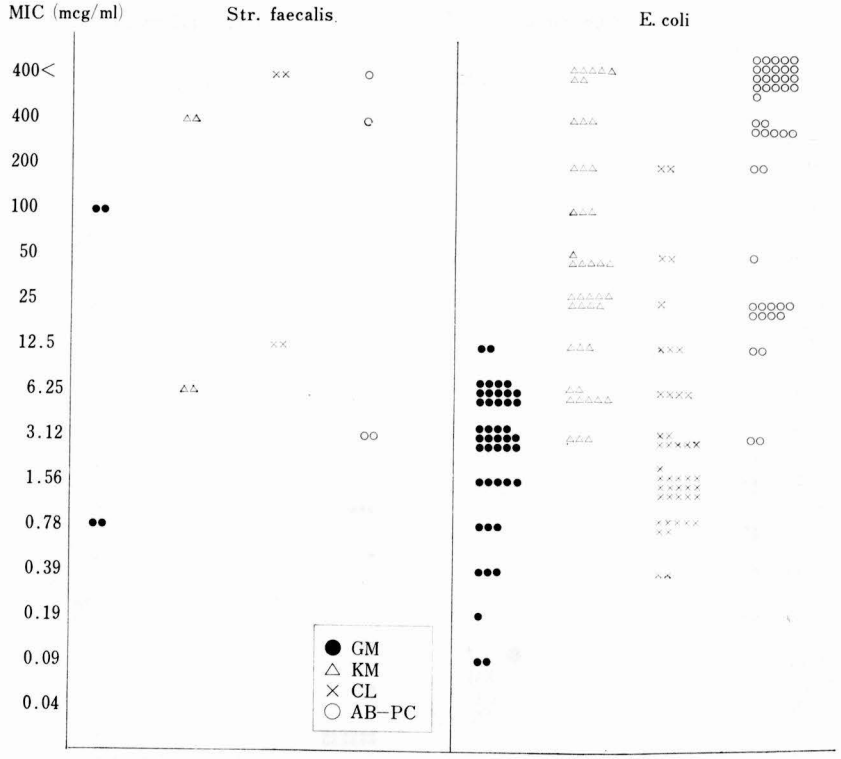
2) *Staphylococcus epidermidis*

Gentamicin gave a high sensitivity distribution below 0.09 mcg/ml for 18 of 24 strains. Next to this was KM, for which there were 2 strains with MIC of 6.25 mcg/ml and 25 mcg/ml, respectively.

3) *Streptococcus faecalis*

As shown in Fig. 2, MIC for GM was 100 mcg/ml for 2, and 0.78 mcg/ml for 2 of 4 strains, indicating the results of which were similarly parallel with the data by the disk sensitivity tests. MIC's for KM, CL or AB-PC were slightly higher than that to GM.

Fig. 2 MIC ranges for *Str. faecalis* and *E. coli*.



No. of strains sensitive or insensitive to test drugs (by disk method).

Str. faecalis	GM	KM	CL	AB-PC	E. coli	GM	KM	CL	AB-PC
sensitive	2	2	2	2	sensitive	44	32	44	18
insensitive	2	2	2	2	insensitive	0	12	0	26

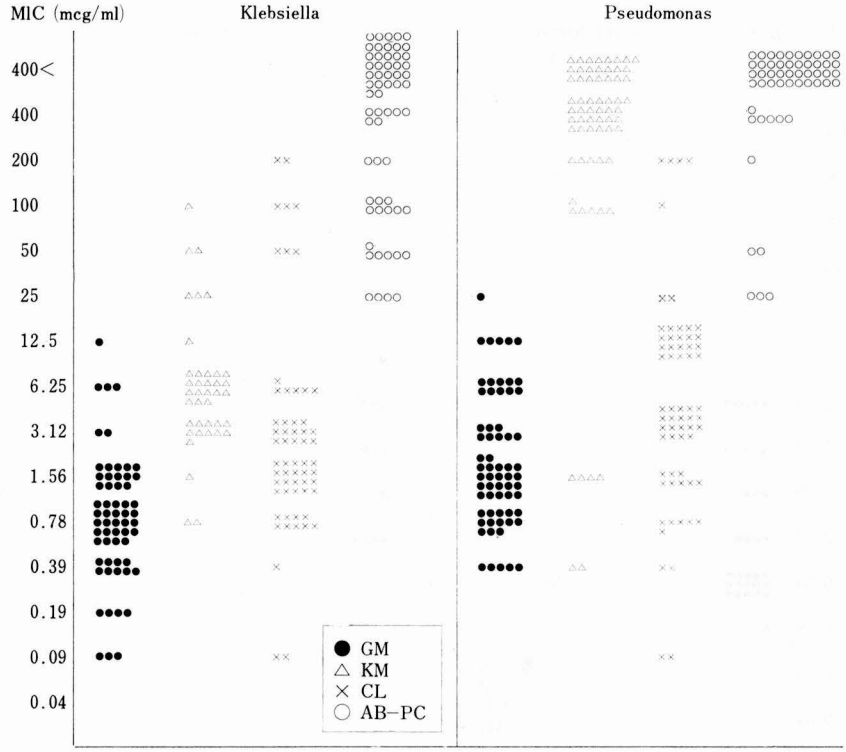
4) *Escherichia coli*

MIC for GM exhibited a peak value of 3.12 mcg/ml for all but one strain as shown in Fig. 2. This indicates that GM gives a more satisfactory sensitivity distribution than those of CL, KM and AB-PC.

5) *Klebsiella*

With the peak at 0.78 mcg/ml, the MIC values were distributed gradually moving downwards. The drug gave an apparently more satisfactory sensitivity distribution than other three agents, as judged by the disk method.

Fig. 3 MIC ranges for *Klebsiella* and *Pseudomonas*.



No. of strains sensitive or insensitive to test drugs (by disk method).

Klebsiella	GM	KM	CL	AB-PC	Pseudo-monas	GM	KM	CL	AB-PC
sensitive	60	38	60	12	sensitive	64	14	64	4
insensitive	0	22	0	48	insensitive	0	50	0	60

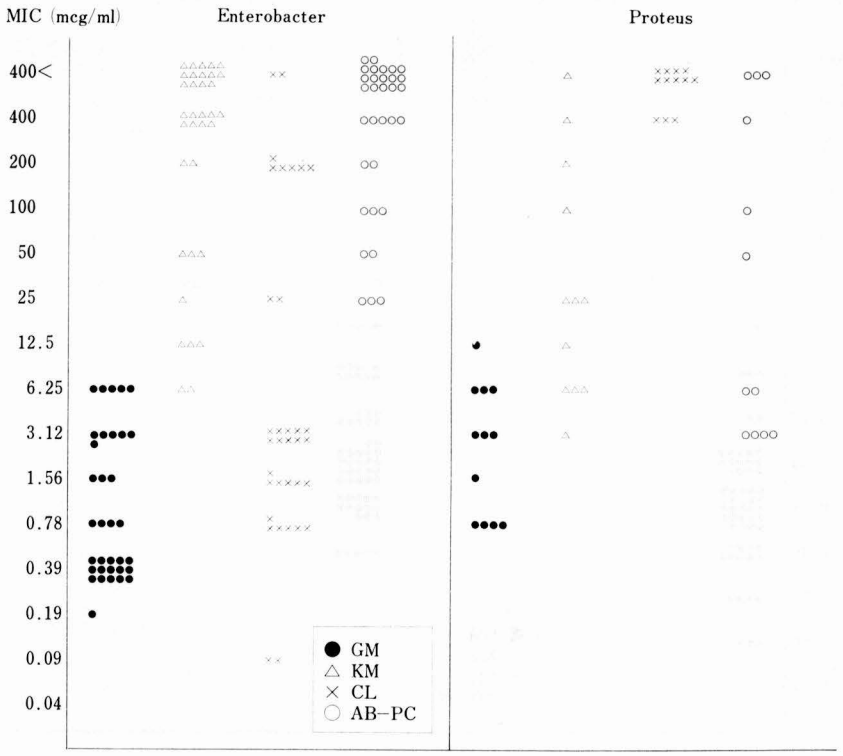
6) *Pseudomonas*

The MIC for GM varied from 12.5 to 0.39 mcg/ml with the peak at 1.56 mcg/ml, except for one strain which MIC gave MIC of 25 mcg/ml, as shown in Fig. 3. It is difficult to compare GM with CL based on such a distribution. Noteworthy, however, in this respect was the fact that there were 4 strains giving the MIC for CL of 200 mcg/ml. Disk sensitivity was positive for all of 64 strains.

7) *Enterobacter*

With the peak at 0.39 mcg/ml, MIC values were all below 6.25 mcg/ml as shown in Fig. 4, giving an evidence of high GM-sensitivity of this organism as confirmed by the disk method. The tendency indicated a significant difference between GM and other three agents.

Fig. 4 MIC ranges for *Enterobacter* and *Proteus*.



No. of strains sensitive or insensitive to test drugs (by disk method).

Enterobacter	GM	KM	CL	AB-PC	Proteus	GM	KM	CL	AB-PC
sensitive	34	8	32	8	sensitive	12	8	0	8
insensitive	0	26	22	26	insensitive	0	4	12	4

8) *Proteus*

GM-MIC was below 6.25 mcg/ml for all but one strain which gave a value of 12.5 mcg/ml. This is compatible with the high GM-sensitivity of the organism as revealed by the disk method.

DISCUSSION

The development of chemotherapeutic agents has brought profound modifications in the picture of infection, resulting, for example, in predominance of gram-negative bacilli, especially *E. coli*, *Klebsiella*, *Pseudomonas* and *Proteus*, as isolates from various clinical specimens. GM has been reported to have a potent antimicrobial activity against these kinds of organisms. We examined GM-sensitivity of the organisms isolated in our laboratory during one year from September 1972 to August 1973.

The disk method was applied throughout the study, and MIC estimation was also done by the use of randomly selected strains.

The data of disk method revealed that:

1) The gram-positive bacteria displayed high sensitivity to the drugs, except for *Str. faecalis*. *Staphylococcus* in particular proved sensitive in 99.4% of the isolates. The incidence of sensitivity was as high as 82.0% for all the strains tested. It was thus found that the gram-positive organisms examined have, in most cases, a significantly higher sensitivity to GM than to other chemotherapeutic agents, especially KM.

2) *E. coli*, *Klebsiella*, *Pseudomonas*, *Enterobacter* and *Proteus-Providence* represent the main components of gram-negative organisms isolated, accounting for 92.0% of all the strains. These organisms were all highly sensitive to GM, and significantly more sensitive than to CL, KM or AB-PC.

The incidences of GM-sensitive strains were 99.7% for *E. coli*, 95.3% for *Pseudomonas* and 99.3% for *Klebsiella*. *Proteus*, in particular, gave a GM-sensitivity rate as high as 94.6% as compared with a low value of 12.6% to CL. The same rate of sensitivity was 97.6% for all the strains tested. The estimation of MIC for individual kinds of organisms led to the following conclusions.

3) The MIC was, in general, below 1.56 mcg/ml for the gram-positive organisms.

4) Among the gram-negatives, *E. coli* gave a MIC below 3.12 mcg/ml. A similar value was obtained for *Klebsiella*. The MIC varied generally from 12.5 to 0.39 mcg/ml for *Pseudomonas* except for one strain (giving MIC of 25 mcg/ml), and fell short of 6.25 mcg/ml for *Enterobacter* and *Proeteus*. This indicates that GM is superior to the other chemotherapeutic agents tested in respect to the range of MIC in all but a few exceptional cases. The drug sensitivity evaluated in terms of MIC does not necessarily correspond for the same strains to that judged by the disk method. Concerning the strains used in this study, it was confirmed that GM exerts a high antimicrobial activity irrespectively of the procedures employed for evaluation.

Finally, it is of interest and importance from clinical points of view to study whether or how the antimicrobial activity of GM will be changed in future in accordance with the frequent clinical use.

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REFERENCES

1. Burger, R. G., Sidell, S. and Kirby, M.M. Ann. Int. Med. 1963. 59. 5. 593/604. Laboratory and clinical studies of Gentamicin, a new broad spectrum antibiotics.
2. Goto, S. et al. Chemotherapy. 1967. 15. 4. 293/297. (in Japanese with English summary) In vitro evaluation of Gentamicin.
3. Ishigami, J. et al. Chemotherapy. 1967. 19. 4. 401/407. (in Japanese with English summary) Use of Gentamicin in Urilogy.
4. Ishiyama, S. et al. Chemotherapy. 1967. 15. 4. 361/369. (in Japanese with English summary) A clinical and clinicolaboratory studies on Gentamicin.
5. Kawamori, U. et al. Chemotherapy. 1967. 15. 4. 232/238. (in Japanese with English summary) Laboratory and clinical studies on Gentamicin.
6. Klein, J. O., Eickhoffff, T. C. and Finland, M. Amer. J. Med. Sci. 1964. 248. 5. 528/543. Gentamicin : Activity in Vitro and observations in 26 patients.
7. Lao, R. L. and Jackson, G. G. J. A. M. A. 1964. 189. 11. 817/822. Gentamicin sulfate, new antibiotic agents against gramnegative bacilli.
8. Mashimo K. et al. Chemotherapy. 1967. 15. 4. 293/297. (in Japanese with English summary) Laboratory and clinical studies on Gentamicin.
9. Mitsuhashi, S. Chemotherapy. 1967. 15. 4. 475/476. (in Japanese with English summary) Susceptibility responce of clinically isolated bacterial strains to Gentamicin.
10. Nakamura, M. et al. Chemotherapy. 1967. 15. 4. 469/474. (in Japanese with English summary) Sensitivity of several gram-negative bacilli from clinical isolates to Gentamicin and more factors influenced on the test.
11. Okubo, H. et al. Chemotherapy. 1967. 15. 4. 401/407. (in Japanese with English summary) Basic and clinical studies on Gentamicin.
12. Shibata, K. et al. Chemotherapy. 1967. 15. 4. 373/377. (in Japanese with English summary) Laboratory and clinical experience on Gentamicin in surgery.
13. Shimizu, K. et al. Chemotherapy. 1967. 15. 4. 282/287. (in Japanese with English summary) Laboratory and clinical studies on Gentamicin.
14. Tsuchiya, T. et al. Chemotherapy. 1967. 15. 4. 467/468. (in Japanese with English summary) Studies on the sensitivity test of Gentamicin.
15. Weinstein, M. J., Luedemann, G. M., Oden, E. M. and Wayman, G. H. Antibacterial agents and Chemotherapy. 1973. 127. Gentamicin a new broad spectrum Antibiotics complex.