COMBINED EFFECT OF PEPSIN-TREATED HUMAN IMMUNOGLOBULIN AND ANTIBIOTICS *IN VITRO*

AKIRA KOSHIRO, JUNKO UCHIYAMA, YUTAKA MATSUSAWA and TADASHI KOUCHIYAMA
Department of Pharmacy, Yamaguchi University Hospital

(Received, February 5, 1982)

Apart from immunological response *in vivo* when combined dose of antibiotics and immunoglobulin is given, the effect of antibiotics upon *in vitro* antibacterial activity resulting from the addition of pepsin-treated human immunoglobulin (GGP) was studied on eight strains of gram positive cocci and gram negative bacilli. An enhanced antibacterial activity due to GGP addition was comfirmed in either cases of minimum inhibitory concentration (MIC), number of bacterial colony, and proliferation curve. It was very interesting phenomenon, in particular, that the effect was also seen in each case of *Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella pneumoniae*, being moderately or more resistant to antibiotics. This phenomenon also was verified through microscopic morphological observation.

INTRODUCTION

The superiority in combined administration of antibiotics and immunoglobulin preparation in severe infection, which dates back to FISCHER and MANNING[1], has been substantiated through various laboratory data, whereas there is no elucidated mode of action except such conjectural participation in some defense mechanism of a living body as facilitation in phagocytosis due to activation of complement.

UEDA et al.[2] detected the activity in combination of several antibiotics including chloramphenicol and others with immunoglobulin on nutrient agar plate through which increase of the resistance in *Staphylococcus* was inhibited. ZWISLER and JOACHIM[3] also reported that combination of ampicillin and immunoglobulin preparations in Mühler-Hinton media inhibited the occurrence of mutants of *Staphylococcus aureus* resistant to ampicillin. These facts are considered to be interesting phenomena with different mode of action from those assumed through *in vivo* activities.

However, both aforementioned reports were so simple and insufficient to obtain detail of the experiment.

Therefore, using commercially available pepsin-treated human immunoglobulin preparation (GGP) as immunoglobulin, we have studied the detail combined effect of GGP and antibiotics *in vitro* and also made microscopic observation.

MATERIALS AND METHODS

GGP: 2.5 g/vial of Gamma-Venin®, supplied by Hoechst was used. One vial contained immunoglobulin 2.5 g, aminoacetic acid 1.25 g and sodium chloride 0.42 g. The main component of immunoglobulin comprises IgG 2.15 g and IgA 0.35 g, while IgM and complement being negative.

Antibiotics: Ampicillin (ABPC), cephalothin (CET), carbenicillin (CBPC) and minocycline (MINO) were supplied by Fujisawa, Shionogi, Fujisawa, and Lederle, respectively.

Organisms: *S. aureus* 25, 100 and 400 (resistant to ABPC 25, 100 and 400 μg/ml, respectively) clinically isolated were submitted by Department of Clinical Pathology of Yamaguchi University Hospital. Three strains of standard bacteria (*E. coli* NIHJ JC-2, *K. pneumoniae* ATCC 27736 and *P. aeruginosa* ATCC 9721) and two strains of bacteria clinically isolated (*E. coli* 2235 and *K. pneumoniae* 3296), were submitted by the Central Research Laboratory of Shionogi.

Antibacterial experiment on additives: Following three strains of *S. aureus* and five strains of gram negative bacilli (Table 1) were preincubated overnight at 37℃ in Tripticase Soy Broth (TSB, BBL), one loopful precultures of the former and

Table 1 Materials and concentration of pepsin-treated human immunoglobulin used in this study

Organism	Antibiotic	Concentration of GGP %
S. aureus 25	Ampicillin	0
S. aureus 100		0.5
S. aureus 400		1
		2
E. coli NIHJ JC-2	Cephalothin	0
E. coli 2235	Carbenicillin	2
K. pneumoniae ATCC 27736	Minocycline	4
K. pneumoniae 3296		
P. aeruginosa ATCC 9721		

GGP : pepsin-treated human immunoglobulin preparation

the latter were inoculated onto the plates of Heart Infusion Agar (HIA, Difco) prepared as media to which 1% of aminoacetic acid plus 0.33% of sodium chloride, and 2% of aminoacetic acid plus 0.67% of sodium chloride were added, respectively. The suspensions obtained were subjected to overnight culture at 37℃ to determine number of viable bacteria, which compared with those on HIA media, as control, not containing aminoacetic acid and sodium chloride.

Measurement of Minimum Inhibitory Concentration: The minimum inhibitory concentration (MIC) was measured in accordance with the standard method of the Japan Society of Chemotherapy[4].

Count of colony: Plates were prepared as the same in measurement of MIC. The test bacteria were preincubated for 18 hours at 37℃ in TSB to prepare ten-fold diluent, and each 0.1 ml of which was inoculated onto media. Colonies were counted following 24 hours incubation at 37℃. HIA, as a control, was used against culture media which contains antibiotics alone, while those containing GGP alone which indicate corresponding concentration to the subject were employed for the control against media containing antibiotics and GGP.

Proliferation curve: Each test strain was subjected to overnight preincubation at 37℃ in TSB, and one loopful of which was incubated by shaking for three hours at 37℃. This bacterial suspension was added into culture medium which contains GGP plus antibiotic demonstrating MIC of 10^6 CFU/ml inoculation in Table 2 (GGP concentration was 1% for *S. aureus* and 2% for gram negative bacillus), and the mixture of 10^6 CFU/ml obtained was incubated by shaking at 37℃ to count number of bacteria after 1, 2, 4, 6 and 24 hours.

MIC determination of bacteria after 24 hours shaking culture: After counting of bacterial number at 24 hours in the above proliferation curve experiment, *E. coli* NIHJ JC-2 and *K. pneumoniae* ATCC 27736 were collected immediately to determine antibacterial activity, and the MICs were compared with those prior to 24 hours shaking culture.

Statistical analysis: A. Significance of MIC decrease due to GGP addition was judged by χ^2 test.

B. The result from the determination of colony was processed as follow; Total 17 culture media in serial two-fold dilution (10 culture media in case of *S. aureus*) initiated from 1,600 μg/ml of antibiotics concentration (12.5 μg/ml for *S. aureus*) were compared with those in GGP added cases where colonies decreased to half or more of the control, and expressed by percentage. The result obtained is shown as decrement of colony, using this value of which the significant difference resulting from presence or absence of GGP was decided by χ^2 test.

C. Of the proliferation curve, the significant difference educed through addition or without addition of GGP was judged by Student's t-test using logarithmic conversion value of viable bacteria at 2, 4 and 6 hours.

Microscopic observation: *S. aureus* 25 and *K. pneumoniae* 3296 were used as the test strains which were subjected to overnight preculture at 37℃ using TSB, and each one loopful of the culture was inoculated into Heart Infusion Broth (HIB, Difco) to perform shaking culture at 37℃ for one hour, following which such two procedures as A and B described below were carried out using bacterial suspension on the way to logarithmic growth phase.

A. Observation by means of a phase contrast microscope

A film agar medium of ABPC 6.25 μg/ml plus 1% of GGP and a film agar medium of CET 25 μg/ml

Table 2 Decrease of MIC caused by addition of pepsin-treated human immunoglobulin preparation

Organism	Anti-biotic	GGP conc. (%)	10^8 CFU/ml* MIC(μg/ml)	10^8 CFU/ml* P† (%)	10^6 CFU/ml* MIC(μg/ml)	10^6 CFU/ml* P† (%)
S. aureus 25	ABPC	0	25		0.78	
		1	25		0.78	
		2	12.5	vs. 0&1	0.20	vs. 0&1
S. aureus 100	ABPC	0	100		1.56	
		1	100		1.56	
		2	50		0.39	vs. 0&1
S. aureus 400	ABPC	0	400		12.5	
		1	400		12.5	
		2	50	vs. 0&1	1.56	vs. 0&1
E. coli NIHJ JC-2	CET	0	25		12.5	
		2	6.25	vs. 0	3.13	vs. 0
		4	0.05	vs. 0&2	<0.025	vs. 0&2
	CBPC	0	12.5		12.5	
		2	3.13	vs. 0	1.56	vs. 0
		4	0.20	vs. 0&2	<0.025	vs. 0&2
	MINO	0	12.5		6.25	
		2	3.13	vs. 0	3.13	vs. 0
		4	0.025	vs. 0&2	<0.025	vs. 0&2
E. coli 2235	CET	0	800		50	
		2	400	vs. 0	25	vs. 0
		4	6.25	vs. 0&2	1.56	vs. 0&2
	CBPC	0	>1,600		>1,600	
		2	>1,600		>1,600	
		4	>1,600		100	vs. 0&2
	MINO	0	50		25	
		2	50		12.5	
		4	3.13	vs. 0&2	0.78	vs. 0&2

Organism	Anti-biotic	GGP conc. (%)	10^8 CFU/ml* MIC(μg/ml)	10^8 CFU/ml* P† (%)	10^6 CFU/ml* MIC(μg/ml)	10^6 CFU/ml* P† (%)
K. pneumoniae ATCC 27736	CET	0	12.5		3.13	
		2	3.13	vs. 0	1.56	
		4	0.39	vs. 0&2	0.05	vs. 0&2
	CBPC	0	>1,600		200	
		2	400	vs. 0	50	vs. 0
		4	25	vs. 0&2	25	vs. 0&2
	MINO	0	12.5		6.25	
		2	6.25	vs. 0	3.13	
		4	3.13	vs. 0&2	1.56	vs. 0&2
K. pneumoniae 3296	CET	0	800		100	
		2	800		50	vs. 0
		4	400	vs. 0&2	0.78	vs. 0&2
	CBPC	0	>1,600		>1,600	
		2	>1,600		>1,600	
		4	>1,600		400	vs. 0&2
	MINO	0	400		100	
		2	200	vs. 0	100	
		4	100	vs. 0&2	50	vs. 0&2
P. aeruginosa ATCC 9721	CET	0	>1,600		>1,600	
		2	>1,600		>1,600	
		4	>1,600		>1,600	
	CBPC	0	200		25	
		2	25	vs. 0	12.5	vs. 0
		4	12.5	vs. 0&2	3.13	vs. 0&2
	MINO	0	50		50	
		2	50		25	vs. 0
		4	25	vs. 0&2	12.5	vs. 0&2

GGP : Pepsin-treated human immunoglobulin preparation

* Inoculum size, one loopful of 10^8 CFU/ml and 10^6 CFU/ml.

† Significant difference determined by χ^2 test using contingency table. $P<0.05$.

plus 4% of GGP were prepared on the slide glasses, and one loopful of *S. aureus* and that of *K. pneumoniae* suspension were inoculated onto the former and the latter, respectively. The resultants obtained were shielded with covering glass and sealed with paraffin. As control, a film agar not containing GGP was prepared to process on the same manner. These specimens were incubated at 37℃, and observation was made and photography taken using a phase contrast microscope (Nippon Kogaku K. K.) every 30 minutes.

B. Observation using a transmission type electron microscope

The collected test bacteria was pre-fixed with 1% glutar-aldehyde solution, followed by fixation with 1% OsO_4. Following which the mixture was dehydrated with alcohol series and embedded with epoxy resin through the method of LUFT[5]. After double staining of the section, being made by LKB 8800 ultra microtome III, with uranyl acetate and lead citrate, observation was made and photography taken using a JEM-100 B transmission type electron microscope (JEOL).

RESULTS AND DISCUSSION

Effect of additives:

It has been reported that aminoacetic acid inhibits growth of *S. aureus*, *E. coli* and *P. fluorescens*[6]. Examination regarding the aminoacetic acid and the sodium chloride, additives contained in GGP showing high level of two concentrations concerned, proved unchanged bacterial number in all kinds of test bacteria as compared to that in control culture medium, thus verified no effects of additives upon growth of these test bacteria.

Effect of GGP addition upon MIC of antibiotics:

Significant decreases of MICs due to the GGP addition were observed regardless of the bacterial inoculum size and/or the bacterial straines. Espe-

Table 3 Decrease of colonies caused by addition of pepsin-treated human immunoglobulin preparation

Organism	Antibiotic	GGP conc. (%)	Decrement of colony (%)	P* (%)	Organism	Antibiotic	GGP conc. (%)	Decrement of colony (%)	P* (%)
S. aureus 25	ABPC	0	66.67			CET	0	64.71	
		0.5	83.33				2	70.59	
		1	100.00	vs. 0&0.5			4	100.00	vs. 0&2
S. aureus 100	ABPC	0	50.00		*K. pneumoniae* ATCC 27736	CBPC	0	29.95	
		0.5	83.33	vs. 0			2	47.06	
		1	100.00	vs. 0&0.5			4	76.47	vs. 0&2
S. aureus 400	ABPC	0	16.67			MINO	0	58.82	
		0.5	33.33	vs. 0			2	64.71	
		1	50.00	vs. 0&0.5			4	64.71	
E. coli NIHJ JC-2	CET	0	52.94		*K. pneumoniae* 3296	CET	0	35.29	
		2	58.82				2	52.94	
		4	100.00	vs. 0&2			4	94.12	vs. 0&2
	CBPC	0	70.59			CBPC	0	0.00	
		2	76.47				2	5.88	
		4	94.12	vs. 0&2			4	58.82	vs. 0&2
	MINO	0	76.47			MINO	0	29.41	
		2	82.53				2	29.41	
		4	100.00	vs. 0&2			4	58.82	vs. 0&2
E. coli 2235	CET	0	41.18		*P. aeruginosa* ATCC 9721	CET	0	0.00	
		2	47.06				2	0.00	
		4	64.71				4	0.00	
	CBPC	0	0.00			CBPC	0	52.94	
		2	0.00				2	58.82	
		4	100.00	vs. 0&2			4	64.71	
	MINO	0	52.94			MINO	0	47.06	
		2	52.94				2	47.06	
		4	76.47	vs. 0&2			4	52.94	

GGP : Pepsin-treated human immunoglobulin preparation

* Significant difference determined by χ^2 test using contingency table. $P<0.05$.

cially, marked combined effects against highly resistant straines i.e. three strains of *S. aureus*, *E. coli* 2235, *K. pneumoniae* 3296 and *P. aeruginosa* ATCC 9721 were noticed (Table 2).

Effect of GGP upon number of colony:

In order to examine the effect of GGP addition on bacterial proliferation, decrement of colony (D. C.) calculated was compared (Table 3). The result obtained means that the antibacterial response of culture medium containing GGP and antibiotic becomes more favorable as numerical value of D. C. increases.

With regard to the three strains of *S. aureus*, D.C. in the case of 1% GGP addition was significantly greater than that in the cases of 0.5% and non-addition ($P<0.05$).

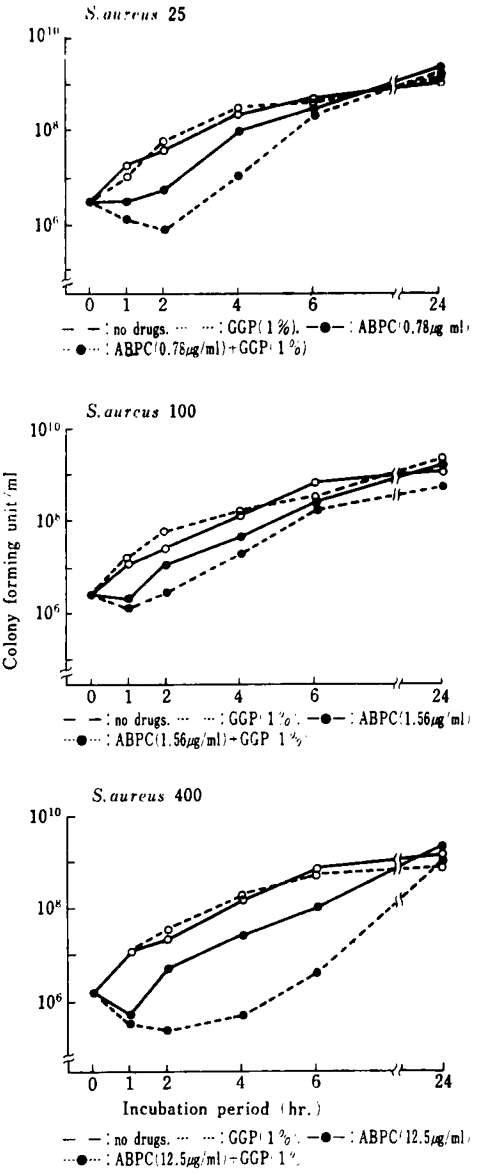
Effect of GGP addition against each strain of *E. coli* and *K. pneumoniae* was also observed in the three kinds of antibiotics (CET, CBPC and MINO) to which 4% of GGP was added individually, demonstrating significant increases of D.C. as compared with D.C. in addition of 2% GGP and none ($P<0.05$) except that combined effect with CET could not be detected against *E. coli* 2235.

P. aeruginosa ATCC 9721 is highly resistant to CET and also poorly sensitive to CBPC and MINO and the effect of GGP addition upon D.C. was observed in neither cases of 2% nor 4%.

Effect of GGP addition upon proliferation curve:

In order to examine the effect of GGP addition, the proliferation curves on two kinds of HIB to which antibiotic alone and antibiotic plus GGP were added were illustrated (Fig. 1), and number of viable counts of bacteria at each time of 2, 4 and 6 hours was compared. Figure 1 and 2 also illustrate the proliferation curve on each HIB containing GGP alone and none of added drugs serving as control. The GGP concentrations were determined as 1% for the three strains of *S. aureus* and 2% for the other bacteria. Viable counts of bacteria at 2, 4 and 6 hours on HIB to which GGP alone was added were compared with that on HIB to which none of drugs were added. Significant difference could not be observed with the test bacteria and confirmation was made of these levels of additional GGP in that no impeded proliferation of these bacteria was noticed. Although concentration of ABPC added to the three strains of *S. aureus* was different,

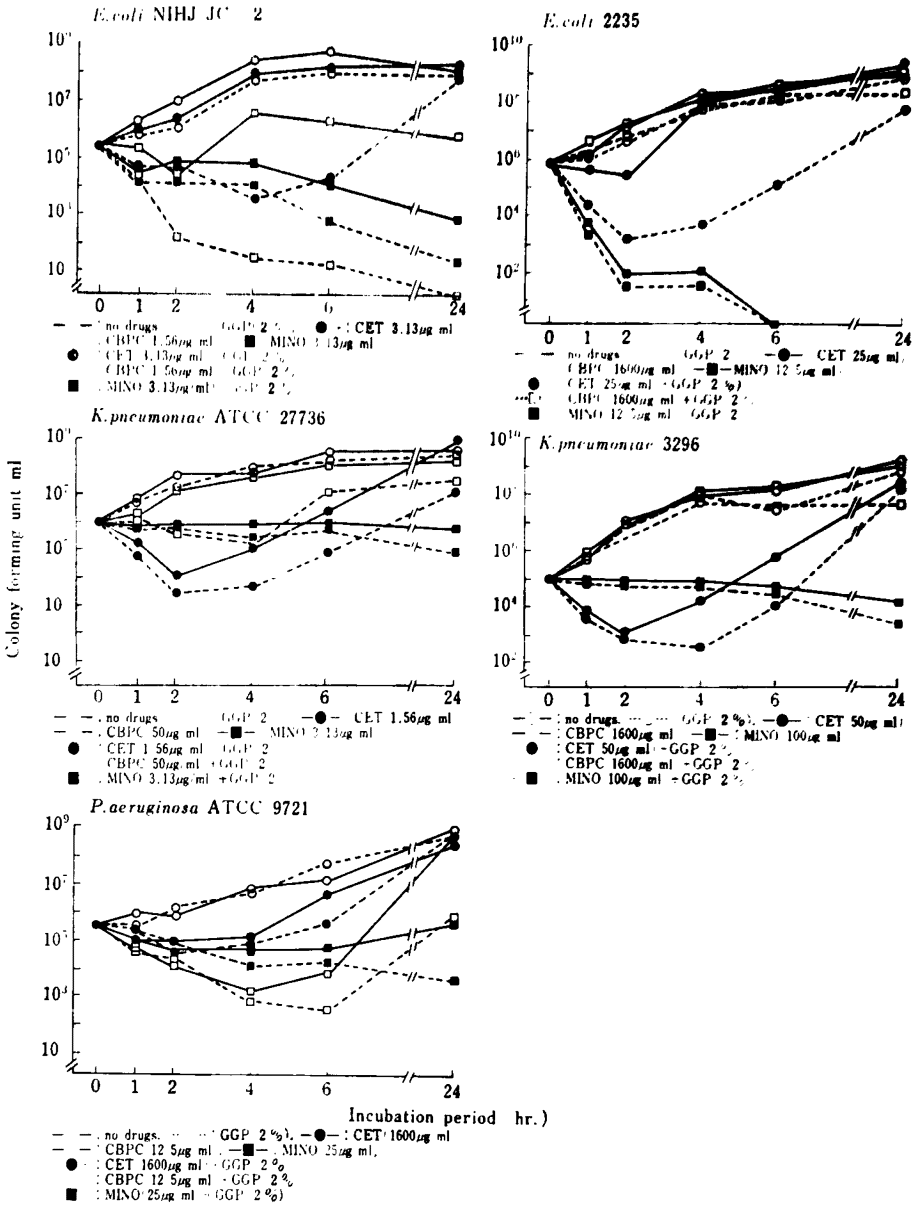
Fig. 1 Combined effect of antibiotics and pepsin treated human immunoglobulin preparation against growth curve of bacteria.
GGP: pepsin-treated human immunoglobulin preparation



number of viable bacteria on HIB containing antibiotic plus 1% GGP was significantly fewer than that of control (containing antibiotic alone) at 2, 4 and 6 hours ($P<0.05$).

Similar inhibiting effects on proliferation due to GGP addition were significant ($P<0.05$) against *E. coli* NIHJ JC-2 (CET and CBPC at 2, 4 and 6

Fig. 1 continued



hours), *E. coli* 2235 (CET at 4 hours) and *K. pneumoniae* ATCC 27736 (CBPC at 4 hours). In the other cases, no significant decrease of number of viable bacteria due to GGP addition was detected, however a tendency indicating some discrimination of viable cells was revealed.

MIC of test bacteria after shaking culture for 24 hours:

In the proliferation curve resulting from shaking culture for 24 hours, regrowth of bacteria was observed in culture media containing β-lactam antibiotics. Since this regrowth phenomenon also was observed on the standard bacteria, i.e., *E. coli* NIHJ JC-2 and *K. pneumoniae* ATCC 27736, MICs on these two kinds of bacteria after 24 hours shaking culture were compared with those shown in Table 2. However, there was no change in MICs between before and after shaking culture. Therefore, regrowth phenomenon is assumed to be attributable to activation in proliferation of a

Fig. 2 Phase contrast micrographs of *S. aureus* 25.
a: Untreated cells, b: Cells treated with ABPC (6.25 μg/ml), c: Cells treated with GGP (1%), d: Cells treated with ABPC (6.25 μg/ml) and GGP (1%).
Bar=5 μm, GGP: pepsin-treated human immunoglobulin preparation

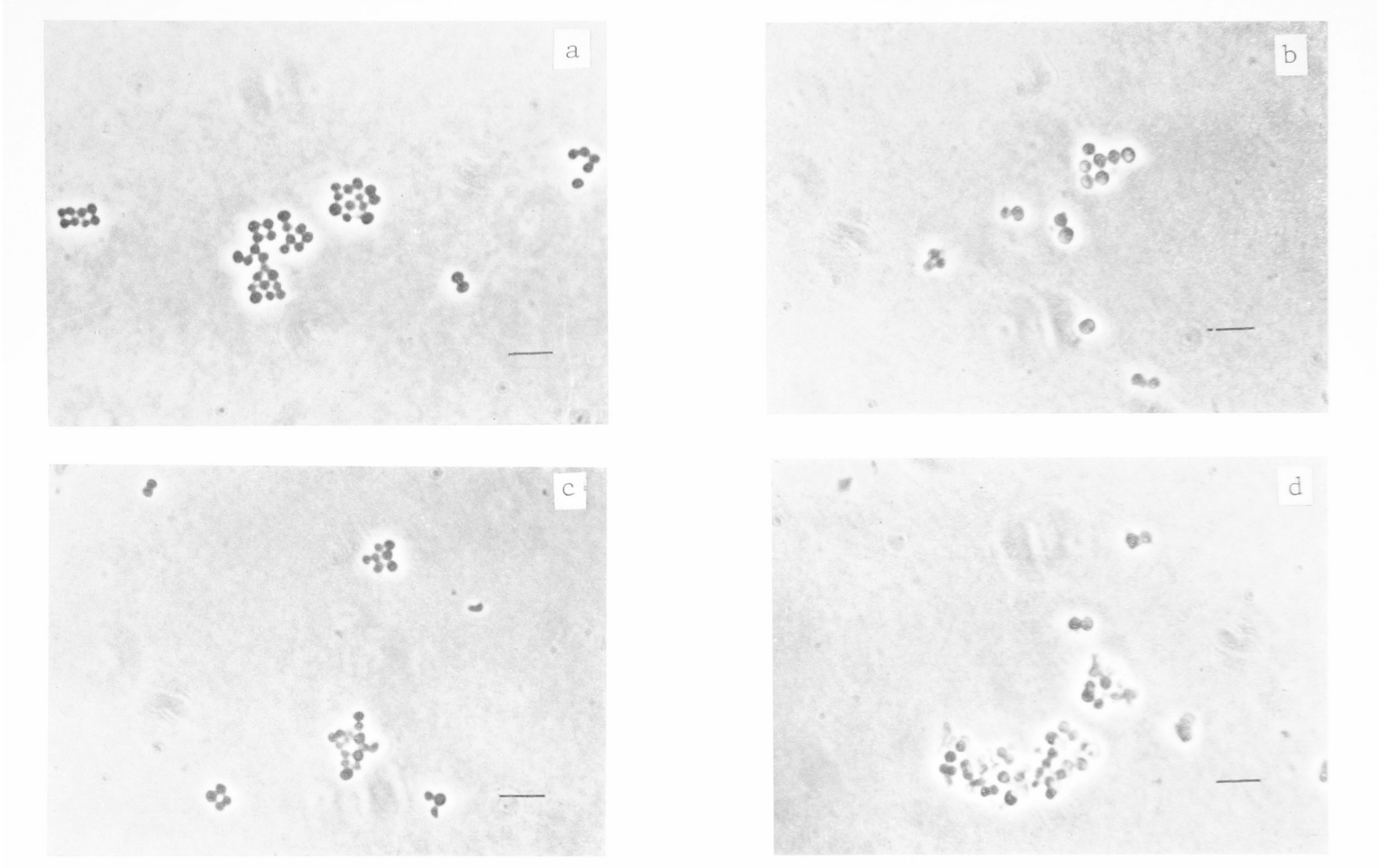


Fig. 3 Electron micrographs of ultrathin section of *S. aureus* 25.
a: Untreated cells, b: Cells treated with ABPC (6.25 μg/ml), c: Cells treated with GGP (1%), d: Cells treated with ABPC (6.25 μg ml) and GGP (1%).
Bar=0.1 μm, GGP : pepsin-treated human immunoglobulin preparation.

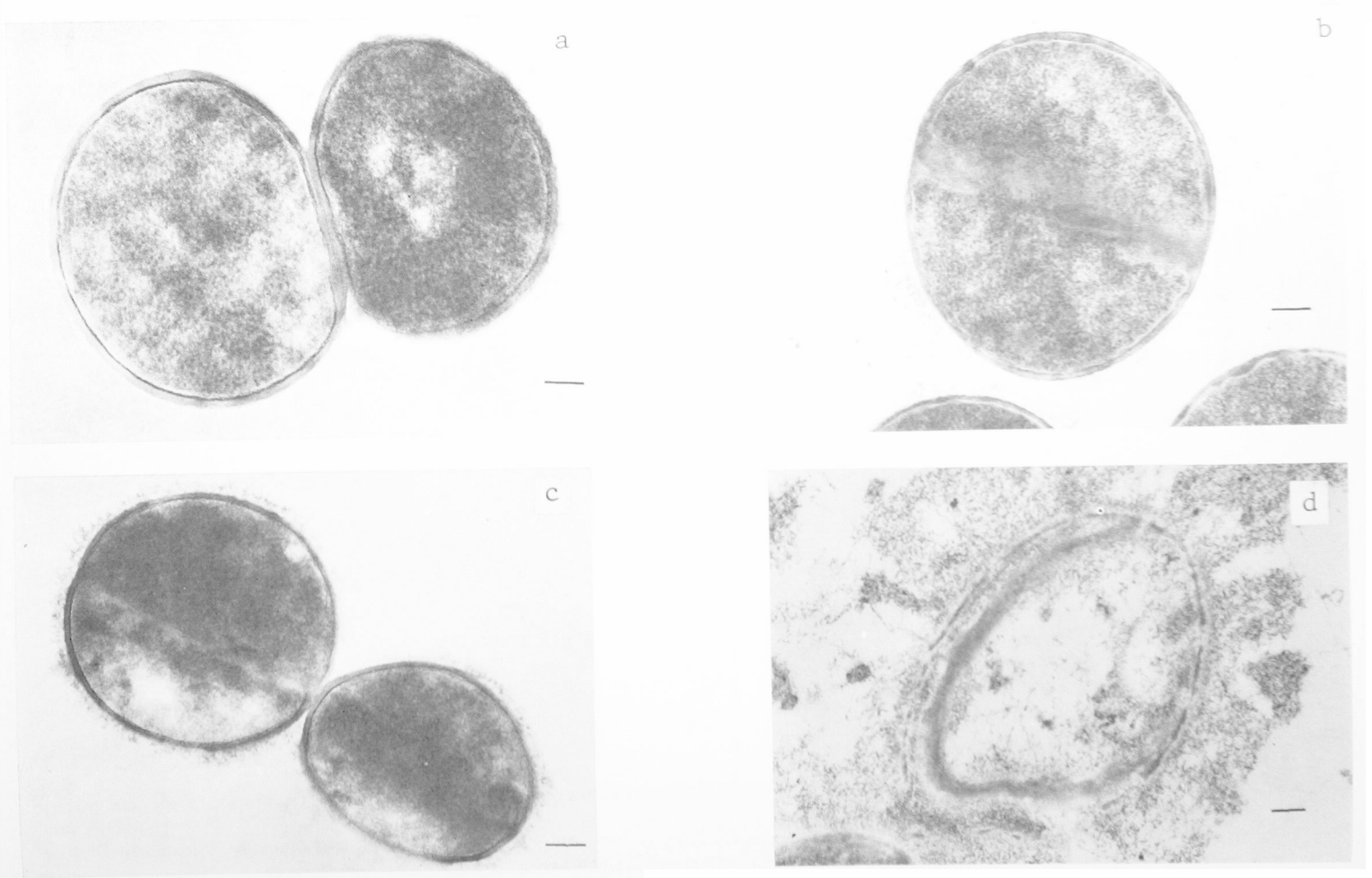


Fig. 4 Phase contrast micrographs of *K. pneumoniae* 3296.
a: Untreated cells, b: Cells treated with CET (25 μg/ml), c: Cells treated with GGP (2%), d: Cells treated with CET (25 μg/ml) and GGP (2%).
Bar=5 μm, GGP : pepsin-treated human immunoglobulin preparation

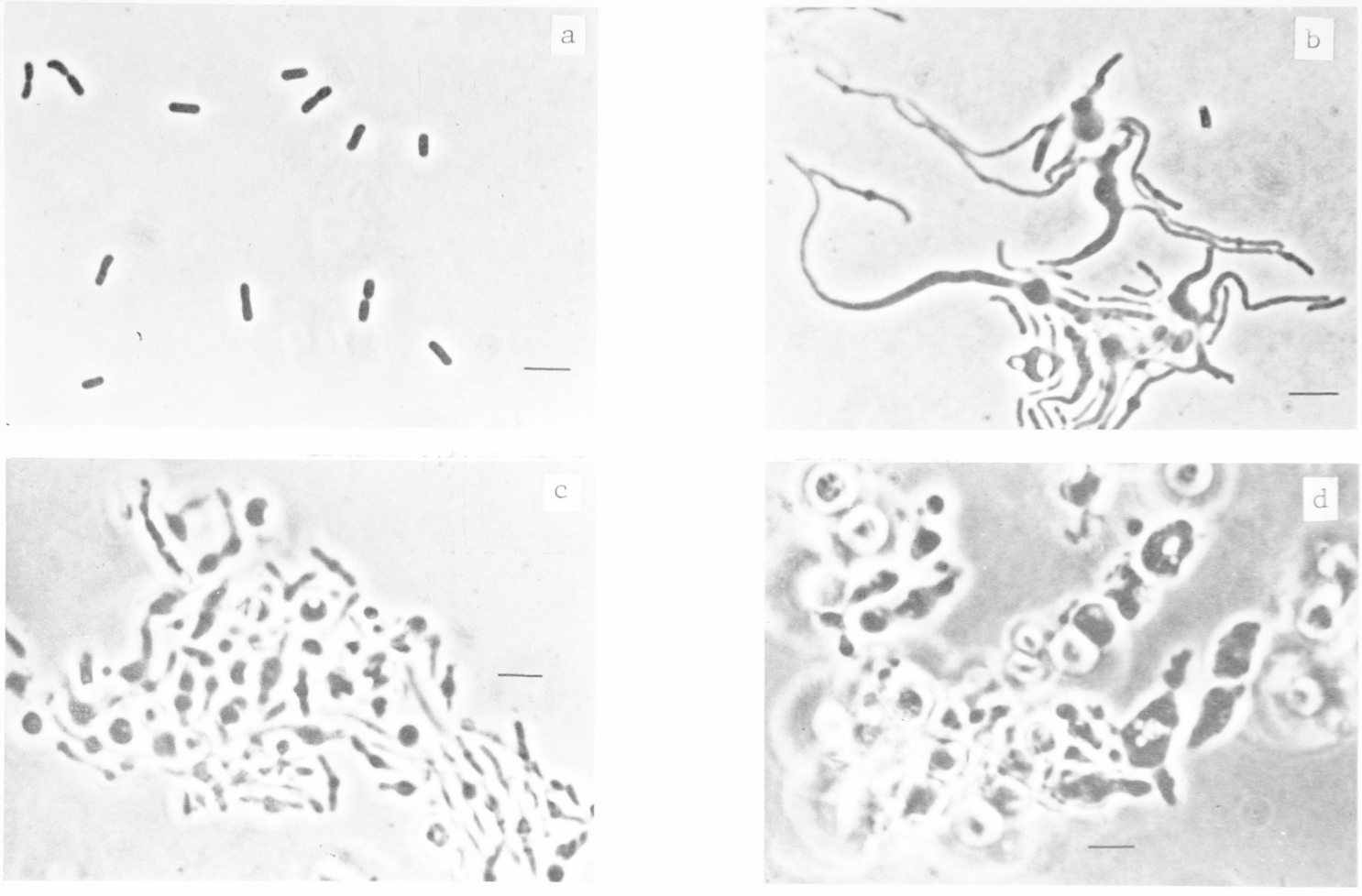
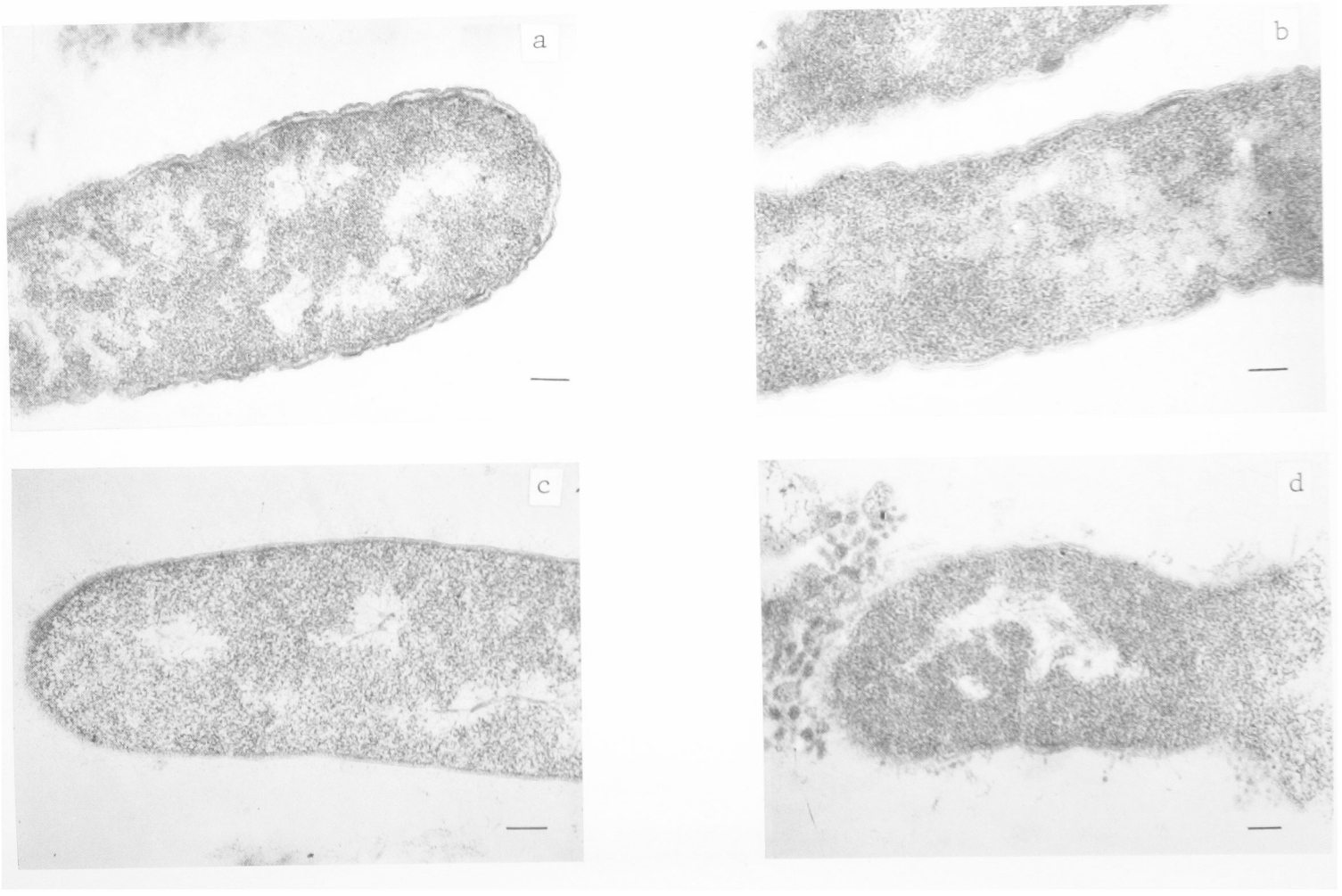


Fig. 5 Electron micrographs of ultrathin section of *K. pneumoniae* 3296.
a: Untreated cells, b: Cells treated with CET (25 μg/ml), c: Cells treated with GGP (2%), d: Cells treated with CET (25 μg/ml) and GGP (2%).
Bar=0.1 μm, GGP : pepsin-treated human immunoglobulin preparation



very small number of bacteria showing poor sensitivity to antibiotics which exist in bacterial suspension. IGUCHI et al.[7] have reported the similar phenomenon of *P. aeruginosa* on culture media containing aminoglycoside antibiotics.

Effect of GGP addition on bacterial morphology:

It has been clarified through the above experiment that addition of GGP to antibiotics enhances antibacterial activity for each test bacteria. No morphological study has been reported on such combined action of GGP and antibiotics. Then, *S. aureus* 25 and *K. pneumoniae* 3296 were subjected to elucidate their morphological changes at one hour after addition of the drugs using a phase contrast microscope (Fig. 2 and 4) and a transmission type electron microscope (Fig. 3 and 5).

S. aureus 25: 2c is a finding after 1% of GGP was added and slight bacteriolysis was found. 2d, where remarkable bacteriolysis was observed as compared with 2c, is a finding when 1% of GGP was added to 6.25 μg/ml of ABPC. 3c, finding of ultrathin section of *S. aureus* 25 where 1% of GGP was added, and being similar to 3a showed slightly thin cell wall and fibrous substances which adhered on the cell surface. In contrast to findings of 3a~c, change in 3d where 1% of GGP was added to 6.25 μg/ml of ABPC was tremendous, i.e., the cell wall was cut into pieces in several places, and the most of the cell content flowed out, covering around of bacteria which allowed the inner parts of bacteria to be diluted. Fig. 3c indicated the cell wall becoming thinner due to addition of GGP, it therefore is conjectured that addition of GGP to ABPC gives some influence on formation of the septum to facilitate bacteriolysis.

K. pneumoniae 3296: 4a is a normal cell finding, and when 25 μg/ml of CET corresponding to 1/4 MIC was added, spheroplast like structure was observed as is shown in 4b. 4c, a finding in the case where 4% of GGP is added, and filament formation is not so remarkable as is shown in 4b, revealed many spheroplast like structure along with partial bacteriolytic finding. Furthermore, addition of 4% GGP to 25 μg/ml of CET resulted in genesis of numerous spheroplast like structure and lysis of most bacteria was shown in 4d.

In section finding of Fig. 5c in the case of 4% GGP added, bacteria whose content partly exuded were observed. Likewise in the case of *S. aureus*, fibrous materials were adhered on the cell surface. 5d is a section finding followed addition of 4% GGP to 25 μg/ml of CET, and where exudation of the content due to the damage of cell wall is noted. Apart from minor granules of the exuded content, agglutination of small granules was observed at the left end of the photograph.

As mentioned above, the antibacterial activity *in vitro* was aparently enhanced through addition of GGP to antibiotics. In particular, noteworthy is the fact that the antibacterial activity was enhanced against gram negative bacilli, highly or moderately resistant to antibiotics, i.e., *P. aeruginosa* ATCC 9721, *E. coli* 2235 and *K. pneumoniae* 3296 clinically isolated. Remarkable morphological changes of bacteria also could be detected using microscopic observation. ZWISLER and JOACHIM[3] reported that normal IgG preparation showed the combined action on *S. aureus* in the presence of ampicillin, so IgG preparations other than GGP are supposed to give the similar combined effect with some kinds of antibiotics. Therapeutic effect of the combined administration of antibiotics with human immunoglobulin preparation has been reported[8)~11)], however it is very interesting that similar combined effect was apparently observed *in vitro* study. The further study will be reported in the following paper.

ACKNOWLEDGEMENT

The authors wish to express their deep thanks to professor HIDEYO KATSUNUMA of Tokyo Medical College for his guidance on electron microscope, and to assistant professor TERUKO NAKAZAWA of Yamaguchi University, School of Medicine for her guidance on the experimental technique and kind advice, and also to Mr. NOBUO IKEUCHI for his helpful discussion on statistical analysis.

REFERENCES

1) FISCHER, M. W. & M. C. MANNING: Synergism between human gamma globulin and chloramphenicol in the treatment of experimental bacterial infections. Antibiot. Chemother. 2 : 315~321, 1957
2) UEDA, Y.; K. HASEGAWA & H. YAZAKI: Combined effect of antibiotics and gamma globulin. Chemotherapy 7 : 13~14, 1959
3) ZWISLER, O. & I. JOACHIM: The effect of gamma globulin preparations in reducing the number of ampicillin resistant mutants of *Staphylococcus aureus*. Diagnostik & Intensivtherapie 2 : 11~14, 1978

4) Japan Society of Chemotherapy: Revision on the measurement of minimum inhibitory concentration(MIC). Chemotherapy 29 : 76～79, 1981
5) LUFT, J. H.: Improvements in epoxy resin embedding methods. J. Biophys. Biochem. Cytol. 9 : 409～414, 1961
6) WAKE, F.; M. IZUMIMOTO, M. MIKAMI & H. MIURA: On the bacteriostatic action by glycine. Res. Bull. of Obihiro Univ. 9 : 159～160, 1974
7) IGUCHI, H.; T. NISHINO, T. YAMADA, T. HORIKAWA & S. NAKAZAWA: Bacteriological evaluation of tobramycin, A new aminoglycoside antibiotic. Chemotherapy 23 : 843～858, 1975
8) KNOUF, E. G.: The combined use of gamma globulin and chloramphenicol in the treatment of refractory infections. Antibiot. Annu. 585～592, 1957—1958
9) SCHONHOLTZ, G. J.; C. A. BORGIA & S. J. RITCHEY: The combined use of gamma globulin and broad spectrum antibiotics in the treatment of osteomyelitis. A preliminary study. Antibiot. Annu. 635～642, 1958—1959
10) HAYAKAWA, H.: Clinical application of gamma globulin preparations. J. Pediatr. Practice (Japan) 32 : 1135～1141, 1969
11) SHIBATA, K.; T. KATO & M. FUJII: Chemical effects of gamma globulin for intravenous injection for surgical infections resistant to antibiotics. Chemotherapy 18 : 991～999, 1970

ペプシン処理ヒト免疫グロブリンと抗生剤の *in vitro* 併用効果

神代　昭・内山　純子・松沢　豊・河内山　正
山口大学医学部附属病院薬剤部

免疫系を含まない実験系において，ペプシン処理ヒト免疫グロブリン（GGP）の添加による，抗生剤の *in vitro* 抗菌作用への影響を，グラム陽性球菌，陰性桿菌8株について検討した。MIC，細菌集落数，増殖曲線のいずれにおいても，GGP 添加による抗菌作用の増強が確認された。特に高度ないし中等度耐性の *P. aeruginosia*, *E. coli*, *K. pneumoniae* についてもこの効果がみられたことは非常に興味ある現象である。また，この効果は顕微鏡による形態観察によっても認められた。