# Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated at Fukuoka University Hospital

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We evaluated 97 cases of infection by methicillin-resistant *Staphylococcus aureus* at the Fukuoka University Hospital, where this infection presents a serious problem. We evaluated the origin of specimens, coagulase typing, production of toxic shock syndrome toxin-1 (TSST-1) and susceptibility to various antimicrobial agents isolated at between February and May 1989. Specimens consisted primarily of sputum and pus. Sixty percent of all strains produced coagulase type VII. Only 4 strains produced TSST-1. Vancomycin, rifampicin, clindamycin, and sulfamethoxazole/trimethoprim showed good antibacterial activities against MRSA. Coagulase type VII strains were resistant to minocycline but sensitive to erythromycin and clindamycin as compared with those of type IV.

**Key words**: MRSA, coagulase type, drug susceptibility

## Introduction

Nosocomial infection produced by methicillin-resistant *Staphylococcus aureus* (MRSA) is a serious problem in our country. In our institution (an 800-bed hospital), MRSA has become a serious problem. Though the hospital staff uses measures to control this infection, its nature changes each year[1]. Coagulase type II strains are becoming the predominant instead of type IV, and are more resistant to various antibiotics than type IV[2,3]. We evaluated the antimicrobial susceptibility, coagulase type and production of TSST-1 of 97 clinical isolates of MRSA between February and May 1989, and identified an outbreak of the coagulase type VII strain of MRSA.

### Clinical isolates

*Staphylococcus aureus* strains were isolated at the central laboratory of our hospital. Clinical isolates were tested for resistance to oxacillin using the disk diffusion susceptibility assay method specified by the National Committee for Clinical Laboratory Standards (NCCLS)[4]. Zone size was read after incubation for 24 hours. Isolates of *S. aureus* with zone sizes $<10$ mm around a disk containing 1 $\mu$g oxacillin were difined as being MRSA. Of these, 100 strains were evaluated, excluding those counted more than once from the same patient.

### Methods

The minimum inhibitory concentration (MIC) of drugs was determined for each strain. Judgement was also made as to coagulase types, and the production of toxic shock syndrome toxin-1 (TSST-1). MIC was measured according to the microdilution method described by the Japan Society of Chemotherapy[5], using frozen plates (Eiken Kagaku & Co. Tokyo, Ltd, Japan). Twelve agents were tested at concentrations of 0.06, 0.12, 0.25, 0.5, 1, 2, 4, 8 and 16 $\mu$g/ml. The agents were methicillin, cefmetazol, imipenem, gentamicin, minocycline, ofloxacin, clindamycin, erythromycin, vancomycin, rifampicin, chloramphenicol, and sulfamethoxazole/trimethoprim. After inoculation with the bacterium, the plates were incubated at 30°C. MIC was then evaluated. Coagulase type and the production of TSST-1 were determined using commertial kits (Denka Seiken & Co. Ltd, Tokyo, Japan).

Statistical analysis for drug susceptibility was

performed using Wilcoxon's t-test. A level of $p < 0.05$ was accepted as statistically significant.

## Results

The total number of strains of *S. aureus* isolated at our central laboratory was 203. Of these, 134 (66%) were methicillin-resistant as determined by disk diffusion assay. We excluded 34 strains which were detected in the same patients. Accordingly, of the remaining 100 strains, 97 strains showed MICs of $>16\ \mu g/ml$ against methicillin by the microdilution method performed at a laboratory in the internal medicine division. Three strains with MICs of $<8\ \mu g/mg$ were excluded from the study. Ultimately, 97 MRSA strains were isolated and evaluated in this study.

**Origin of specimens**

The percentage of the strains categorized by medical department is shown in Fig. 1. The largest proportion, 23.7% (23 strains), was detected on surgery (100 beds), followed by 18.7% (18 strains) from the internal medicine (180 beds). Fourteen strains were isolated from the neonatal intensive care unit (15 beds). Of these, 6 strains were recovered from specimens taken at the time of screening the anterior nares before the patient was discharged from the hospital.

Most of the isolates were cultured from sputum and pus, 38.1% (37 strains) and 35.1% (34 strains), respectively (Fig. 2).

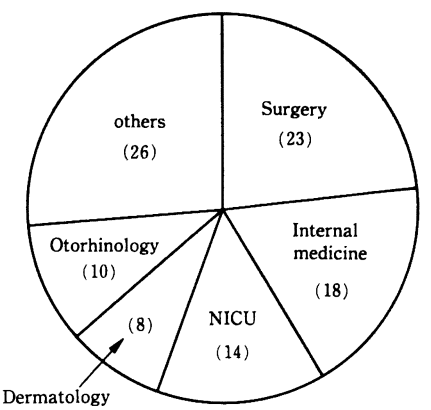



Fig. 1. Distribution of MRSA by medical department.
Total number of strains=97
NICU=neonatal intensive care unit

**Coagulase type**

The distribution of coagulase types appears in Fig. 3. Coagulase type VII made up 61.5% (61 strains), mixed type 9.3% (9 strains), and type VI 6.2% (6 strains). The coagulase type could not be determined in 22.7% (22 strains) even on incubation for 48 hours.

**Production of TSST-1**

Production of TSST-1 was observed in 4 strains. These strains were isolated from the pus of one patient each in the departments of surgery, orthopedics and otorhinology, and from the sputum of

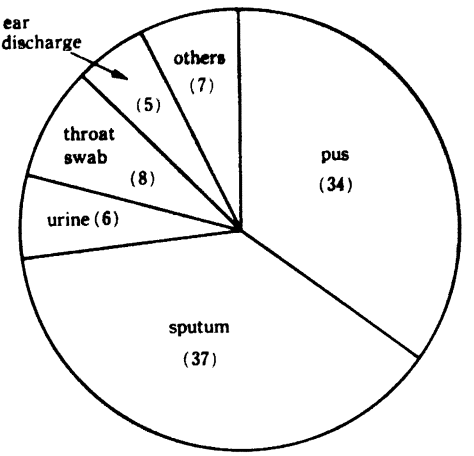



Fig. 2. Distribution of MRSA by specimen.
Total number of strains=97

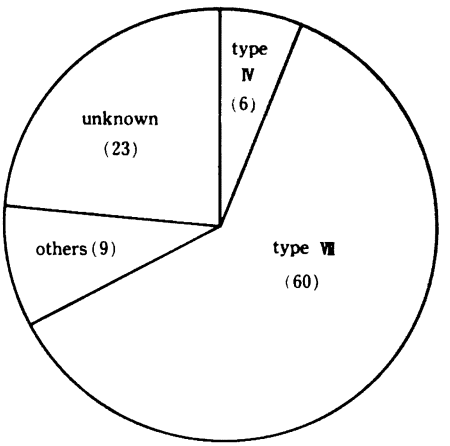
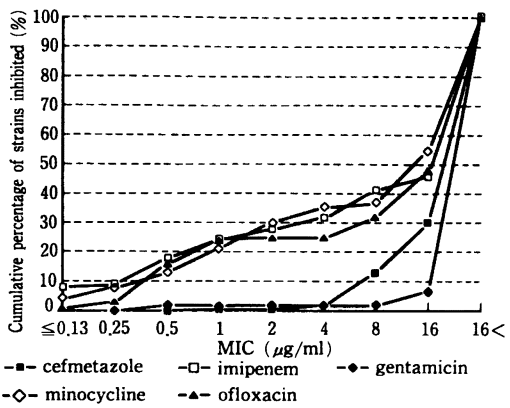



Fig. 3. Coagulase types of MRSA isolated at Fukuoka University Hospital.
Total number of strains=97

one patient in the department of internal medicine.

**Distribution of drug susceptibility**

The distribution of susceptibility to 11 antibiotics appears in Fig. 4. Strains showed bimodal patterns of antimicrobial susceptibility to erythromycin, clindamycin, and ofloxacin. However, no strain was resistant to vancomycin. The $MIC_{80}$s were all 16 $\mu$g/ml or more against minocycline, imipenem and ofloxacin. However, the MICs were 0.13 $\mu$g/ml or less against clindamycin and rifampicin, indicating the good antibacterial activity of these agents. Susceptibility was also satisfactory with erythromycin, ($MIC_{50}$ 1 $\mu$g/ml), vancomycin



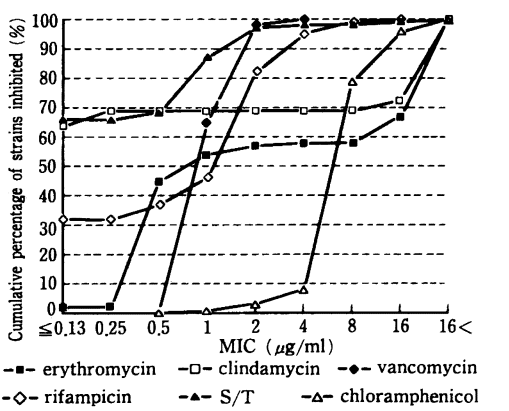




Fig. 4. Susceptibility of MRSA to 11 antibiotics.
a. cefmetazole, imipenem, gentamicin, minocycline, ofloxacin
b. erythromycin, clindamycin, vancomycin, rifampicin, sulfamethoxazole/trimethoprim, chloramphenicol
Total number of strains=97

($MIC_{80}$ 1 $\mu$g/ml), and sulfamethoxazole/trimethoprim ($MIC_{80}$ 2 $\mu$g/ml).

The susceptibility of MRSA strains of coagulase type IV (6 strains) vs. those of type VII (60 strains) to four antibiotics is shown by cumulative MIC curves in Fig. 5. Coagulase type VII were significantly more resistant to imipenem ($p<0.001$) and minocycline ($p<0.05$), and significantly more susceptible to erythromycin ($p<0.001$) and clindamycin ($p<0.05$), than coagulase type IV strains.

## Discussion

MRSA comprized up to 66% of the strains of *Staphylococcus aureus* isolated at our institution. It appears that MRSA is isolated at similarly high rate at other institutions in Japan[6]. However, this rate is higher than reported in the United States[7,8]. The incidence of MRSA was highest in the departments of surgery and internal medicine. The incidence of MRSA in the neonatal intensive care unit (NICU) was also considered high. There is only a small number of beds in the NICU, all infants are screened by nasal culture at discharge. Six infants in whom MRSA strains were isolated were symptom-free and had no inflammatory reaction, indicating a high proportion of MRSA carriers. Most of the specimens studied were sputum and pus. The detection rate was low in urine, blood and feces. Sputum was mainly recovered from non-ambulatory patients with central nerve diseases such as cerebrovascular disorders in the internal medicine division. Pus was mainly recovered from surgical wounds of patients operated on for malignant tumors (data not shown). While 4% of the strains produced TSST-1, no patient developed the toxic shock syndrome. With regard to coagulase type, type VII accounted for 66%, which is markedly higher than previously reported[1~3] Several investigators have reported that MRSA has recently shifted from coagulase type IV to type II[2,3]. A report by investigators at the Kagoshima University Hospital, which is located on the same island as us, stated that coagulase type VII strains account for up to 32.3% of all the MRSA at that facility[9] However, there have been no reports of detection of type VII at such a high rate as in the present study. There was no correlation between coagulase typing and

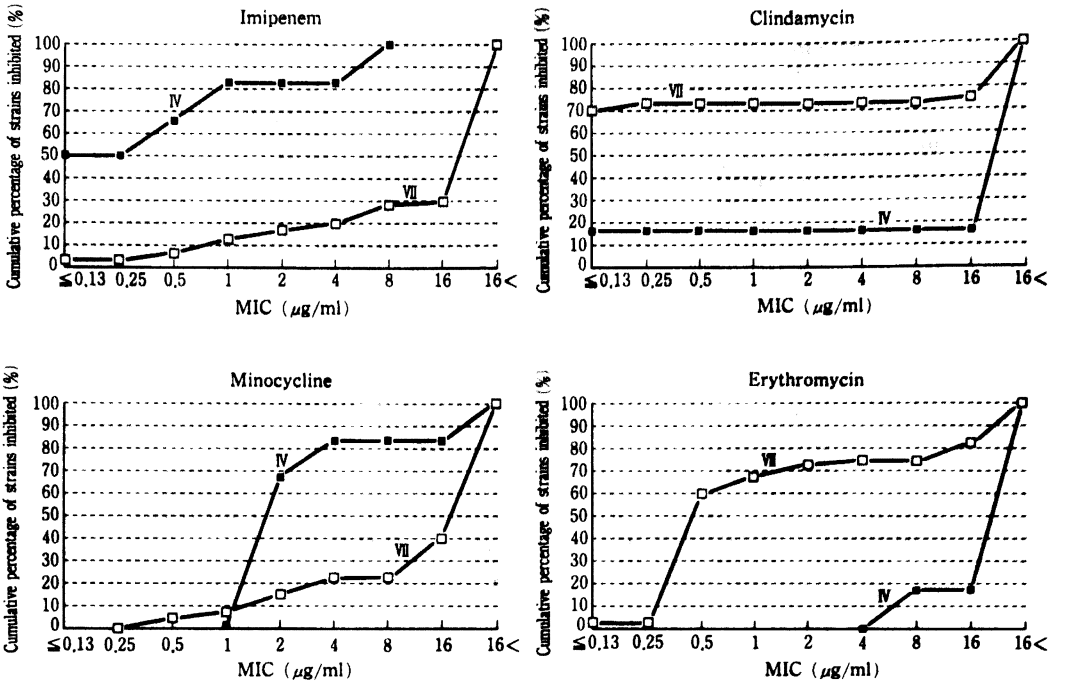



Fig. 5. Susceptibility of MRSA coagulase type IV and VII to four antibiotics.
Number of coagulase type VII strains = 60
Number of coagulase type IV strains = 6

type of specimen (data not shown).

*S. aureus* coagulase type IV is detected mainly in pus from infected wounds and abcesses[10], while type VII is detected more frequently in stool from patients with food poisoning[11]. In our hospital there was no correlation between coagulase typing and type of specimen (data not shown). Further investigation is still required to reveal the cause and epidemiological significance of this high rate of coagulase type VII on Kyushu Island. MRSA clinical isolates in our hospital were resistant to minocycline, ofloxacin and imipenem, but were highly susceptible to erythromycin and clindamycin, even though MRSA is generally thought to be resistant to erythromycin and clindamycin[2] Our correlation between drug susceptibility and coagulase type demonstrated the drug susceptibility patterns of coagulase type VII-producing strains. The infections caused by MRSA strains of coagulase type VII at our facility were sensitive to erythromycin and clindamycin. While several reports have found minocycline to be effective against infections caused by MRSA coagulase type II and IV[3,12], our findings show that erythromycin and clindamycin would be more effective against these strains isolated in our setting.

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## 福岡大学病院において分離された methicillin-resistant *Staphylococcus aureus* (MRSA) 株の検討

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福岡大学病院にて1987年2月から5月までに分離された methicillin-resistant *Staphylococcus aureus* (MRSA) 97株について，検体の由来，コアグラーゼ産生性，toxic shock syndrome toxin-1 (TSST-1) 産生性，種々の抗菌剤感受性について検討した。喀痰と膿が主な分離検体であった。コアグラーゼ型別では，VII型が60%を占めた。TSST-1を産生したのは，4株であった。薬剤感受性では vancomycin, rifampicin, clindamycin, ST合剤が良好な感受性を示した。また，コアグラーゼVII型株は，コアグラーゼIV型株に比して minocycline 耐性，erythromycin および clindamycin 感受性を示した。

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