

# AMDD VOL.6

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## NEWSLETTER

\*English translation of Japanese newsletter

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### **Nosocomial infections with drug-resistant bacteria may occur anywhere**

Nosocomial infections were reported in early autumn 2010, raising the awareness of the general public.

We interviewed Prof. Tetsuya Matsumoto from the Department of Microbiology at Tokyo Medical University to find out more about the drug-resistant bacteria and why we should be cautious about it.

### **Community-acquired MRSA also appears for Staphylococcus aureus**

Methicillin (a penicillin antibiotic)-resistant *Staphylococcus aureus* (MRSA) was first reported in 1961. Since then, various drug-resistant bacteria have appeared, including penicillin-resistant *Streptococcus pneumoniae* (PRSP), ESBL producing bacteria, and vancomycin-resistant *Enterococcus* (VRE). Multi-drug resistant *Acinetobacter baumannii* was first reported in the 1990s, but has recently been a frequent topic of discussion. KPC-producing organisms were also first reported in 1996. Having been reported in 2009, NDM1-producing bacteria have reached pandemic status in India and other areas, a troubling development.

Many different drug-resistant strains of MRSA already exist in the world. A Japan Nosocomial Infection Surveillance (JANIS) in about 10,000 patients under hospitalization in an intensive care unit (ICU), the Ministry of Health, Labor and Welfare revealed that almost one third of the infections were attributable to MRSA, followed by *Pseudomonas aeruginosa* and enterobacteria. Obviously, MRSA is still the most significant bacterium in nosocomial infections. The recent problem with MRSA is bacteria transmission, that is, MRSA carriers are hospitalized and bring the bacteria with them into the institute. Our active surveillance detected MRSA in about 10% of the patients who were hospitalized in emergency medical care centers. About half of the infections could potentially have been

missed if the surveillance had only employed incubation, while the use of PCR (a genetic test) increased sensitivity, which contributed to the results.

Community-acquired MRSA is another concerning form of MRSA infection. It is a form of MRSA that is separated from those who are free from the risk of nosocomial infections, that is, those who have not been hospitalized or treated. The bacteria are mainly prevalent in children and young people. Characteristically, the bacteria may cause pneumonia that can easily become severe, although it mainly leads to skin infections such as impetigo and infections at wound sites. Spread by contact infection, community-acquired MRSA tends to be transmitted at kindergartens and schools, and in particular within sports teams that are subject to frequent physical contact. Community-acquired MRSA tends to respond relatively readily to antibiotic therapies, so treatment is successful in most cases. However, it has been reported that the drug resistance of the bacteria is progressing in other countries. The extent to which this type of bacteria is prevalent in Japan is still unknown. Further analysis is required.

### **Multi-drug-resistant Pseudomonas aeruginosa (MDRP) remains a threat**

Multi-drug-resistant Pseudomonas aeruginosa (MDRP) is a form of Pseudomonas aeruginosa that is resistant to all three systems of antibiotics that were previously very effective for treating Pseudomonas aeruginosa: carbapenem, fluoroquinolone and aminoglycoside. In Japan, there are currently no commercial antibiotics that work on the bacteria when used alone. Effective drugs are only available for treatment if a physician imports them personally.

All parts of the body are susceptible to Pseudomonas aeruginosa, including MDRP. If the neutrophil count drops significantly, an infection will frequently become serious, resulting in septicemia or septic shock in some cases. The ratio of MDRP to Pseudomonas aeruginosa accounts for 1%. Infections can occur at any hospital in Japan, despite being rare. Effective antibiotics are limited for multi-drug resistant Acinetobacter baumannii, KPC-producing organisms and NDM1-producing bacteria besides MDRP. These drug-resistant strains will need further study.

\*The text above is a summary of Prof. Matsumoto presentation at the AMDD 18<sup>th</sup> Media Lecture, prepared by the editorial desk.

Tetsuya Matsumoto, MD, Ph.D  
Director and Professor, Department of Microbiology, Tokyo Medical University

After graduating from the School of Medicine at Nagasaki University in 1987, Prof. Matsumoto joined the second department of internal medicine at the university hospital. He completed the graduate school in 1993 (clinical laboratory medicine). He worked as an assistant at the Faculty of Medicine, Toho University and studied at Harvard University in the United States. He also has served as a lecturer at Toho University. He assumed his current office in 2005 and is a physician accredited by the Japanese Society of Internal Medicine, a specialist/advising doctor accredited by the Japanese Association for Infectious Diseases, and a specialist accredited by the Japanese Society of Laboratory Medicine.

## **In vitro diagnostics that contribute to wellbeing through prevention/diagnosis of diseases**

On August 4, 2010, the American Medical Devices and Diagnostics Manufacturers' Association (AMDD) submitted a position paper to the Ministry of Health, Labor and Welfare jointly with the Japan Association of Clinical Reagents Industries (JACRI) and the European Business Council (EBC). The paper includes the roles of in vitro diagnostics that are indispensable for the prevention, diagnosis, treatment of diseases and observation of prognoses, as well as the issues facing the three industry organizations. In today's interview, we asked Mr. Hisashi Ietsugu, the President of JACRI, for details JACRI's activities and the importance of clinical laboratory tests.

### **From urine test to rapid diagnosis kits**

The Japan Association of Clinical Reagents Industries (JACRI) is an association of corporations that develops, manufactures and distributes in vitro diagnostics essential to medical examinations. The JACRI was founded as a corporate juridical entity with the permission of the Minister of Health and Welfare in May 1989. The current number of member companies is 120, and total sales are in excess of 400 billion yen. We mainly serve domestic medical institutes through pharmaceutical wholesalers, and also export products to overseas customers.

Unlike pharmaceutical products used for treatment and other purposes, in vitro diagnostics (clinical diagnostics) are used for obtaining clinical data useful in medical care from patient blood tissue, cells, excreted urine, feces, phlegm and the like. Clinical laboratory tests are now indispensable for disease diagnosis and treatment determination, although these materials were initially used as a supplementary diagnosis to general examinations such as history taking. In vitro diagnostics are widely used during medical checkups in workplaces or schools, and they play an important role in detecting lifestyle-related diseases at the asymptomatic stage, enabling early treatment.

Today, a rapid diagnosis kit enables prompt, convenient diagnosis for checking whether a patient is infected with the new influenza virus. In addition, diabetic patients are now able to control their blood sugar levels by self-monitoring blood sugar (glucose).

### **Finally going for customized medical care**

Laboratory tests play a major role in early detection/treatment, prevention and monitoring for the prognosis, as well as the diagnosis of diseases and the selection of a treatment regime. Accordingly, our members devote themselves to the development of new inspection technologies and items that utilize state-of-the-art technologies such as genetic analysis. It is our aim to contribute to the health of Japanese, while playing a part in reducing medical expenses. We are working academic societies and organizations standardizing tests to enable patients to take high-quality tests at any medical institute in Japan.

Since genetic analysis became available, individualized medical care (customized medical care) has drawn attention, e.g. the selection of the optimal therapy and pharmaceutical products for each individual patient. Once genes and biomarkers are examined in advance, the highest degree of efficacy is ensured, and the pharmaceuticals with the fewest side effects are administered. This approach has already been tested in fields such as oncology.

In vitro diagnostics used for individualized medical care are called companion diagnostics. However, the supply of companion diagnostics is sometimes delayed drastically because there are no clear criteria for reviewing/approving companion diagnostics. As a result, it is necessary to create an environment in which companion diagnostics can be used, while also developing new therapies and pharmaceuticals. It is an issue of urgency that new review criteria and rules for in vitro diagnostics be developed.

The revised Pharmaceutical Affairs Law, which was implemented in April 2005, incorporates in vitro diagnostics in the pharmaceuticals category, while in vitro diagnostics are strictly regulated, similar to medical devices, for international compliance. If in vitro diagnostic devices and in vitro diagnostic agents were to be integrated into one category, and compliance with international regulations and rules is ensured, this would stimulate the unification of review and assessment methods and the rapid introduction of foreign products into the Japanese market.

### **Review process to be improved and items to be reviewed**

The in vitro diagnostic agent review process requires the approval of the Minister of Health, Labor and Welfare. In addition, a company's application for approval is first forwarded to the Pharmaceuticals and Medical Devices Agency (PMDA). The review is always subject to significant delays at this stage. Statistically, fewer than half of all applications are approved during the review period for in vitro diagnostics, although the PMDA sets the period at six months. In this context, JACRI submitted a position paper to the Ministry of Health, Labor and Welfare jointly with AMDD and EBC in August 2010. The position paper proposes the idea of handling in vitro diagnostics, requesting the improvement of the review process, readjustment of the examination items and a system that allows the examiners from the PMDA to ensure an efficient review.

Our critical mission is to provide healthcare settings with products that are useful for maintaining people's health. However, we are not allowed to use the latest in vitro diagnostics that are available in many other countries. It is unfortunate that Japanese patients are not able to receive optimal treatment based on accurate examination results using leading-edge technologies. The delay in the review process is known as drug lag for pharmaceuticals and device lag for medical devices. In vitro diagnostics share the same problems.

Lifestyle-related diseases and age-related disorders will occur more often, accompanying the ageing population and changes in the lifestyle and the social environment in Japan. Preventing diseases and prolong healthy life expectancy is of the utmost importance. Our association strives to improve the medical welfare of Japanese nationals by understanding and summarizing internal and external problems surrounding clinical diagnostics while cooperating with other related organizations so as to promote a wider range of activities.

Mr. Hisashi Ietsugu  
President, Japan Association of Clinical Reagents Industries (JACRI)

Mr. Ietsugu joined Sanwa Bank, Limited (now Bank of Tokyo-Mitsubishi UFJ, Ltd.) after graduating from the Faculty of Economics at Kyoto University in 1973. Entered Toa Electric Co., Ltd. (now Sysmex Corporation) as a director in 1986. He was appointed President and CEO in 1996 after serving as a member of the managing board/executive managing director. He also currently serves as Vice-Chairman of the Kobe Chamber of Commerce and Industry.

## **Patient's Voice**

### **The pleas of patients' families can reach the government, my story**

By Ms. Kyoko Narimatsu, Director, Honnetto (a group for patients with lateral curvature of the spine)

We set up Honnetto (a group for patients with lateral curvature of the spine) while appealing for the early approval of VEPTR, an orthotic used for the treatment of children with intercurrent congenital lateral spinal curvatures. The disease partially deforms the bones, hindering the growth of the lungs. My daughter began VEPTR treatment when she was four years old (she is now seven). VEPTR is a medical device used to mechanically stabilize and correct a deformed thorax in patients with thoracic insufficiency syndrome and immature bones. At the time, treatment was extremely expensive in Japan because VEPTR had not yet been approved as a medical device.

I blogged about my daughter's growth, and the blog triggered a campaign seeking approval for VEPTR in March 2008. Our voices spread around Japan through an abundance of goodwill via the mass media. On May 19 of the same year, we met Mr. Yoichi Masuzoe, the then Minister of Health, Labor and Welfare, together with the children requiring VEPTR, to convey our heartfelt voices as parents.

As a result of the campaign, during which around 140,000 signatures were collected with the help of numerous people and repeated requests to the Ministry of Health, Labor and Welfare, VEPTR was approved as a medical device on December 22, 2008. I strongly felt that we had achieved what the patients' families desperately wanted. The patients' families got together and continued to appeal earnestly. That appeal generated a great deal of power, even though each individual only had a small amount of power.

Subsequently, to raise awareness of lateral curvature of the spine, we established a patient group in February 2009, and began transmitting information on our website. As of October 2010, the group has attained over 140 members in Japan.

Lateral curvature of the spine treatment requires patients to wear a corset (orthosis) for a long period of time. People often stare at patients if they are not aware of the disease. It's my opinion that the disease places a significant mental burden on the families as well as patients, as I have experienced myself.

I hope that information exchanges and interactions between patients' families and children, and dissemination of accurate information on the lateral curvature of the spine through patient groups, the young children undergoing treatment and their families will be happy. In turn, the suffering of the new patients diagnosed each year and their parents will be reduced as much as possible.

## **Medical Journalist Viewpoint**

### **Constant advances never cease**

By Mr. Yoshizo Ohno, Chairman, Medical Journalists Association of Japan

I am a strong believer in the advancement of medical technology. When I visited a certain medical institute, I only found large diagnostic imaging equipment from the United States or Germany. None of the equipment was made in Japan. The institute told me that it chose American and German equipment because it was better, although it was rather expensive. The Japanese machines had low resolution. I said that I didn't think Japan was technically behind in terms of precision machines. They advised that Japanese machines were not particularly inferior, but they seemed to be technically behind because the manufacturers had focused too much on domestic demand in the 1980s. I then realized that technical progress meant ongoing advances without a break, accompanied by competition. Scientific technology made for the benefit of the public never ceases.

Over forty years ago, there was a committee of masked members, even in such a technically advanced country as America. The committee of secretly appointed masked members selected those who were to be treated, because hemodialysis was not available to everyone at the time. Today in Japan, patients with kidney failure are eligible for dialysis to prevent uremia, which is covered by national health insurance. Almost 300,000 patients are kept alive in this way in Japan. Around 5% of patients undergo ongoing dialysis for more than 25 years. This is the outcome of forty-years of advancement.

In the past, to check for lesions in the stomach and intestines, barium had to be taken for an X-ray examination or patients had to submit a fecal sample to enable observation of occult blood reactions. There was no other choice at the time. Endoscopes have been used to diagnose diseases more frequently in recent years. Physicians and surgeons tend to choose this method more often because disease checks can be carried out accurately as long as the endoscope is manipulated properly. This is part of the advancement as well.

In the past, medical interventions focused on advanced disease treatment. More recently, the focus has been early detection and treatment. There are now more technologies that prolong life as long as early action is taken, even if a patient is suffering from cancer. The large diagnostic imaging equipment that I introduced initially is increasingly used for predicting the occurrence of diseases now, rather than disease detection. Genetic probing is stimulating research around the world to contribute to disease prevention. The ceaseless advances in medical technologies are contributing to prognosis, rather than detection, of diseases, and the pace of advances in diagnostic technologies is realizing the hopes of patients, one after another. I believe that one day, diagnostic technologies will be discovered for cancer and Alzheimer's disease, two common diseases today. The progress of medical technologies never ceases.





## **AdvaMed holds reception introducing new chairman**

The Advanced Medical Technology Association (AdvaMed) held a reception at the Imperial Hotel on November 2, 2010, for the relevant individuals from the Japanese medical device industry. Its purpose was to introduce these individuals to James V. Mazzo (Chairman and CEO of Abbott Medical Optics Inc. (AMO), and Senior Vice President of Abbott Japan Co., Inc.), who was appointed chairman in March of that year.

Chairman Mazzo revealed his ambition to provide advanced medical technology requested by Japanese surgeons and patients and requested an assessment of the necessary innovations for doing so. At the reception, Mr. Seiji Maehara, the Minister of Foreign Affairs, stated that there are excellent technologies and human resources in the United States, and that he believed that cooperation between the United States and Japan would make a valuable contribution to medical care around the world. The party attracted numerous members of the American Medical Devices and Diagnostics Manufacturers' Association (AMDD), the Japanese medical device manufacturers' association, the Ministry of Health, Labor and Welfare, and the PMDA. Everyone celebrated the appointment of the chairman and enthusiastically exchanged opinions on the future of advanced medical technologies in Japan and the United States.

## **AMDD holds second general meeting**

The second general meeting of the American Medical Devices and Diagnostics Manufacturers' Association (AMDD) was held at the Imperial Hotel on September 16, 2010. Prior to the start of the proceedings, Mr. David W. Powell, the Chairman of the AMDD, offered a few words of greeting, stating that the AMDD would provide more healthcare value to Japanese patients and medical professionals in cooperation with member companies. He also said that it would make a strong effort eliminate device lag and device gap in close alliance with the public administration and related organizations. Further, Mr. Powell added, the AMDD was looking forward to its third anniversary.

This year, Prof. Takao Ohki of the Department of Vascular Surgery at the Jikei University School of Medicine gave a special lecture titled, "How AMDD can help Japan? Help me to help you." According to Prof. Ohki, Japan is becoming more and more prepared for international joint research. An international joint study into a cardiovascular device was launched recently with the United States. If clinical trials are performed on just 10% of all cases, the approval process will be accelerated in Japan, helping address device lag. Following the general meeting, a convivial party was held where opinions were energetically exchanged with the representatives of the Ministry of Health, Labor and Welfare, the PMDA and industry organizations.

## **Value of Medical Technology (Orthopedic material)**

### **Materials for repairing the spine**

The spine plays many vital roles, including supporting and moving the upper body and protecting the intestines and ribs. It also protects major nerves such as the spinal cord. Many of the patients in the department of orthopedics have problems with their spines. A recent survey estimates there are 30,000,000 patients with spinal osteoarthritis.

Once the spine suffers problems such as degeneration, deformation, fracture or tumor, a bone or disk may cause pain, or movements of the upper body may be hindered. When nerves such as the spinal cord or spinal nerve root are damaged or compressed, pain, numbness, paralysis and excretion disorders can occur.

Such problems are primarily treated with conservative therapies and surgery tends to be avoided. However, surgery may be selected in some cases. The main purposes of spinal surgery are depressurization and fixation. Depressurization involves eliminating pressure on compressed nerves to alleviate symptoms. During fixation, the fixed site is reinforced using spacers made from artificial material, or metal items including screws and plates.

Because fixing materials are used in locations where the skin is thin, the challenge for manufacturers is to reduce the thickness and/or size and design of fixing material to prevent it from stimulating the skin. In addition, manufacturers are involved in a daily struggle to satisfy various needs, such as the development of surgical apparatuses for minimally invasive surgery (MIS), which exerts less of a burden on the patient's body.

(Written by: Asako Hashimoto, Stryker Japan K.K.)

## **17th and 18th Media Lectures held**

The American Medical Devices and Diagnostics Manufacturers' Association (AMDD) held the 17th Media Lecture on September 29, 2010. Lectures were given on hospital-associated infections (HAI) including nosocomial infections, which are an issue of urgency around the world. Microbiology Prof. Tetsuya Matsumoto of Tokyo Medical University discussed countermeasures to drug-resistant strains of these infections in clinical practice. Dr. Toru Yoshikawa, Deputy Director of the Institute for Science of Labor, provided advice on a technique for preventing needle stick injury.

The 18th Media Lecture was held on November 16 of the same year under the theme of the treatment of prostate hypertrophy and corneal transplantation using the latest laser technology. During the lecture Ms. Junko Kodama, Director of AMDD, explained the laser. This was followed by lectures on state-of-the-art laser procedures by Dr. Osamu Nakano, Deputy Manager of the Department of Urology, Senen Hospital (Tagajo, Miyagi Prefecture), and Prof. Shigeru Kinoshita, Department of Ophthalmology, Kyoto Prefectural University of Medicine. The lectures looked at the outcomes of using recently approved advanced machines, highlighting efficacy and improved patient QOL.

### **Value of Medical Technology**

Our mission is to make more people understand the unlimited potential of advanced medical technology and its contribution to the reformation of the Japanese medical care system

\*All opinions in this newsletter are the personal opinions of the authors, and do not necessarily represent the opinions and activities of AMDD.