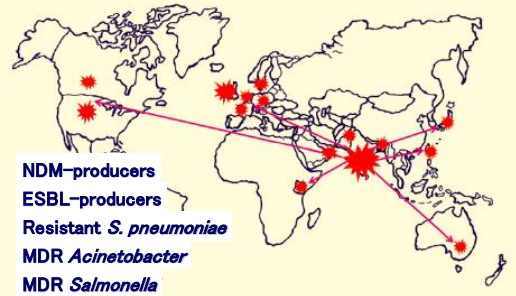


Asia-Pacific Economic Cooperation
 20 September, 2018
 Taipei

Fighting Antimicrobial Resistance with Rapid, Point-of-Need Diagnostic Methods

Kazuhiro Tateda, MD, PhD
 Department of Microbiology and Infectious Diseases
 Toho University School of Medicine, Tokyo, Japan

We are "Epicenter" of Antibiotic Resistant Bacteria



Int J Antimicrob Agents 37: 291, 2011

National Action Plan on Antimicrobial Resistance (AMR)

2016-2020

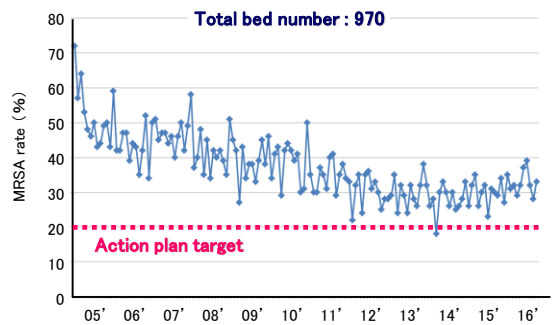


"Mt Fuji Action Plan"
 Higher Goal is good, but

April 5, 2016

The Government of Japan

Percentage of MRSA in total *S. aureus* (all specimens) - Toho University Hospital 2005~2016 -



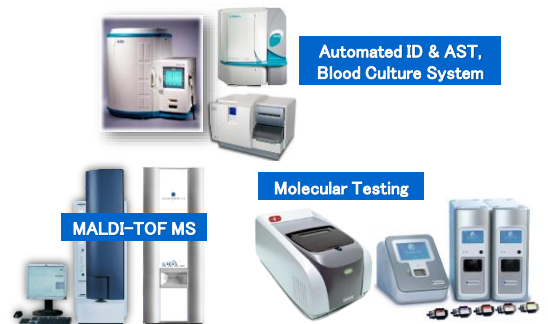
Toho University Hospital

Six Areas and Goals for Countermeasures on AMR

1. Public Awareness and Education
2. Surveillance and Monitoring
3. Infection Prevention and Control
4. Appropriate Use of Antimicrobials
5. Research and Development
6. International Cooperation

National Action Plan on AMR in Japan 2016

"Top 3" Innovation in routine microbiology laboratory



FilmArray® A Game Changer !?

1
Hour

Identify Pathogens from Positive Blood Cultures in About 1 Hour

The FilmArray Blood Culture Identification Panel (BCID) tests for a comprehensive list of 24 pathogens and 3 antibiotic resistance genes associated with bloodstream infections. With just one test you can identify pathogens in 9 out of 10 positive blood cultures in about an hour with only 2 minutes of hands-on time.



Verigene® A Game Changer !?

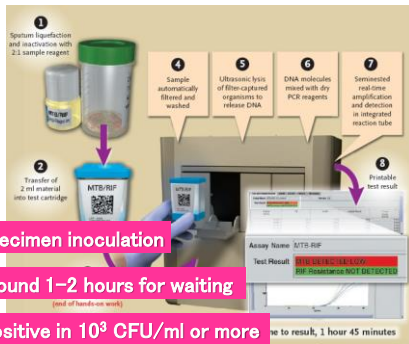


Gram Positive Panel
12 species
Drug Resistance Genes
(*mecA*, *vanA*, *vanB*)

Gram Negative Panel
K. pneumoniae
K. oxytoca
E. coli
P. aeruginosa
Acinetobacter spp.
Enterobacter spp.
Proteus spp.
Citrobacter spp.

5 min handling
and wait for 2.5 hours !

GeneXpert® A Game Changer !?



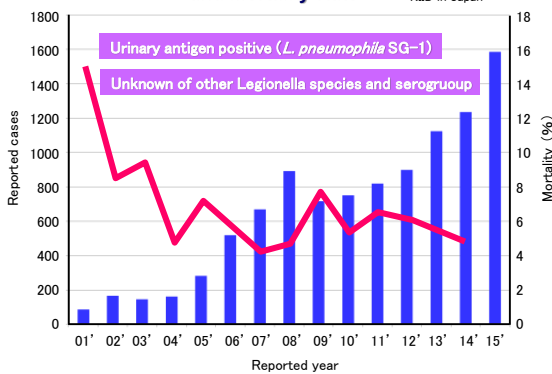
Boehme CC et al. N Engl J Med 363: 1005, 2010

Ideal Diagnostic Methods in AMR era

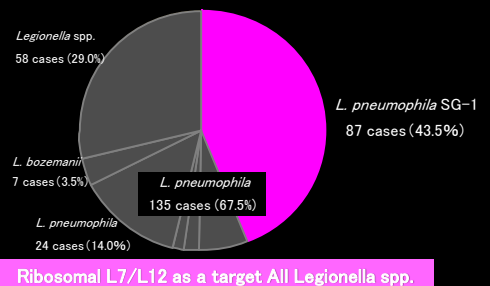
- “Within 30 min” (Before ABX treatment)
- ID for species and AST
- Correlation to severity and/or pathogen load
- Differentiation between Infection and Contamination
- Cost, Cost, Cost, Cost . . .

Improvement for survival . . .

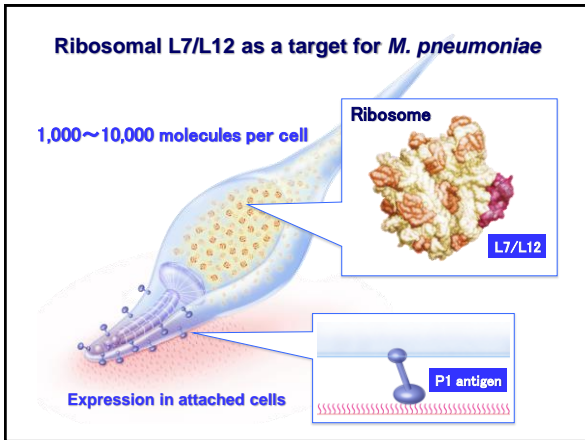
Annual Changes of Legionella Pneumonia Cases and Mortality Rate



Causative Organisms of Legionella Pneumonia (200 cases)

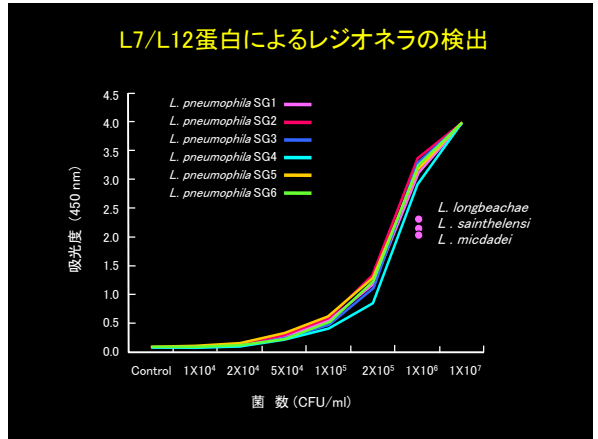
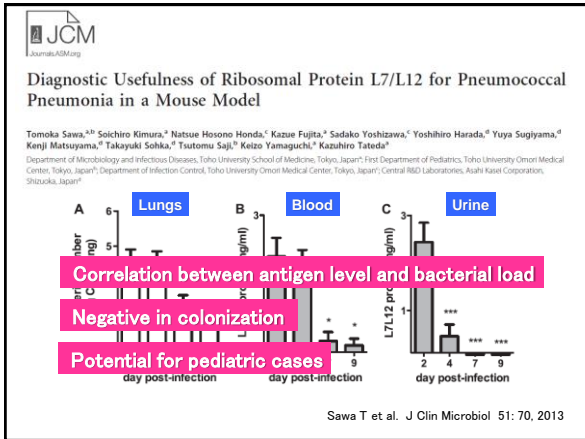


Department of Microbiology and Infectious Diseases
Toho University School of Medicine

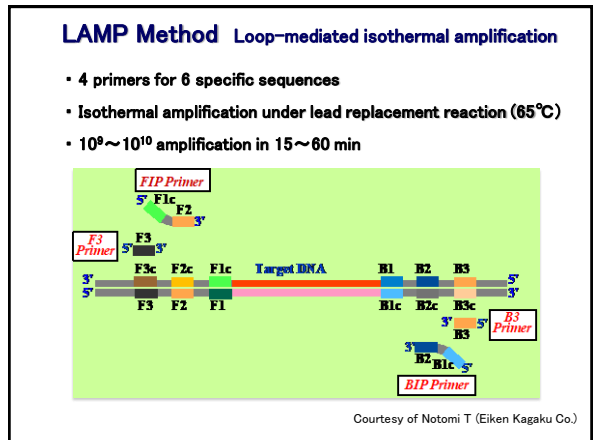


First in the World
Mycoplasma
Rapid Diagnosis Kit

Ribo-Test Mycoplasma
— Targeting Ribosomal L7/L12 protein —



- ### Immuno-, DNA-Chromatography Method
- | | |
|--|---|
| Urine specimens | Respiratory specimens |
| <ul style="list-style-type: none"> <i>S. pneumoniae</i> <i>Legionella</i> spp. <i>S. aureus</i> <i>P. aeruginosa</i> | <ul style="list-style-type: none"> <i>S. pyogenes</i> Adeno virus Influenza virus RS virus <i>S. pneumoniae</i> <i>M. pneumoniae</i> <i>B. pertussis</i> TB and NTM |
| Stool specimens | |
| <ul style="list-style-type: none"> Noro virus Adeno virus <i>E. coli</i> O-157 <i>C. difficile</i> | |



Detection of LAMP Positive Results by Naked Eye

Only 30 min of amplification time for new LAMP instrument

200 100 50 0 CFU/mL

Positive results were observed in 50 CFU/mL or over of *M. tuberculosis* by naked eye

Courtesy of Notomi T (Eiken Kagaku Co.)

Rapid qPCR system "within 10 min"

① Microfluidics ② Miniaturized fluorescence detector

Higher temp. area for denaturalization of DNA Lower temp. area for annealing and extension

Detectable a small amount of virus and bacteria within approximately 10 min.

Furutani, S. et al. Anal Bioanal Chem 408: 5641, 2016
Furutani, S. et al. Meat Science 131: 56, 2017

Rapid qPCR system "within 10 min"

Shortest denaturation Shortest annealing/extension

2 sec for denaturation 5 sec for annealing/extension

Furutani, S. et al. Anal Bioanal Chem 408: 5641, 2016

DNA Chromatography Chip (Kaneka)

"Fast & visual detection device" for multiplex PCR amplicons

Target gene Tag Tagged amplicon Colored particle

Tag Primers (Kaneka patented)

DNA Chromatography Chip (Kaneka)

After PCR, 5 min for detection
High sensitivity (100 times)
Multiplex application available

Nagai S et al. Harmful Algae 51: 97, 2016

"Electronic-Nose" Technology

J Clin Microbiol. 2010 Nov;48(11):4235-8. Epub 2010 Aug 16.
Electronic-nose technology using sputum samples in diagnosis of patients with tuberculosis.
Kolk A, Hoelscher M, Maboko L, Junq J, Kuliiner S, Cauchi M, Bessant C, van Beers S, Dutta B, Gibson T, Reither K.
Curr Opin Pulm Med. 2012 May;18(3):228-32.

Developments in novel breath tests for bacterial and fungal pulmonary infection.
Chambers ST, Scott-Thomas A, Edjon M.
aDepartment of Pathology, University of Otago, Christchurch bDepartment of Infectious Diseases cDepartment of Respiratory Medicine, Christchurch Hospital, Christchurch, New Zealand.

New Diagnostic Methods in “AMR era”

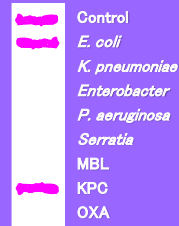
1. Diagnostic Methods

- “within 30 min” to Guide Antibiotic Use
- Bacteria or Virus
- AMR Mechanisms and Antibiotic Choice

2. Development of Novel Antimicrobials

- Narrow, but Potent (Pathogen-directed Therapy)
- Anti-Virulence or Anti-Resistance Therapy
- Immuno-Modulatory Therapy

BSI – POCT



**Not Dream,
Near Future**

Dr. K

“ We suspect sepsis by
KPC-producing *E. coli* “

Make Our Future with
Effort, Insight and Collaboration !