THE FUTURE OF MICROBIOLOGY
The ongoing revolution

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Agenda

- Primary missions
- Background
- Reduction of time for microbial detection and identification
- Non cultural approach & POCT
- Automation of culture process
- Medical microbiologist: the profession
- Key messages
Primary missions

TO IMPROVE THE MANAGEMENT OF INFECTIOUS DISEASE

CONTRIBUTION TO DIAGNOSTIC
- Presence /absence of pathogens
- Identification +/- quantification

CONTRIBUTION TO CHOICE OF ANTIBIOTHERAPY
- Antimicrobial susceptibility testing, identification of resistance mechanisms and resistance genes

SUPPORT TO INFECTION CONTROL
To provide useful, accurate and relevant results
Useful results

POSITIVE IMPACT ON

- Therapeutic decision?
- Optimized management of patients?
- Morbidity, mortality?
- Length of hospitalization?

Reduction of Turn-Around-Time for result and its notification to clinician

- Control of nosocomial infections?
- Antibiotic consumption?
- Control of antimicrobial resistance?
Background

To understand priorities for the future
Medical evolutionary background

Impact factors on development and daily practice of microbiology

- **Economic environment**
  - Cost-effective use of available resources

- **Trained human resources**
  - Population pyramid and labour shortage

- **Medical environment**
  - Increasing emphasis on evidence-based medicine and adherence to guidelines

- **Technological background**
  - Exponential progress: molecular biology and robots

- **Quality assurance, traceability**

- **Global increase of antimicrobial resistance**
Global increase of antimicrobial resistance
Emerging superbug

Invasive isolates in Europe: 2005 vs 2009 (EARSS-ECDC)

Proportion of 3rd generation cephalosporin resistant *Klebsiella pneumoniae* (R+I)

Antimicrobial selective pressure
Abusive use of broad-spectrum antibiotics
Delay to identifying MDR bacteria carrier = bad control of transmission
Challenges greater than ever in all parts of the world

- Numbers of emerging infections
- AND Global increase of antimicrobial resistance
- AND Drug development pipeline for new antibiotics virtually empty !!

THREAT within the next 10 years

Shortage crisis of effective drugs for treating bacterial infection
European research priority

To combat growing problem of antimicrobial R

- Multidisciplinary research
- EU Framework Programmes
  - Studies on molecular mechanisms leading to emergence and spread of R genes
  - Epidemiological studies with aim of developing control and preventive measures
- Translational, clinical and public health research
  - For developing guidelines for evidence-based clinical practice and patient management: for prudent use of antibiotics
European research priority

To combat growing problem of antimicrobial R

- EU Framework Programmes
  - To promote the rational use of antibiotics
    - Mobilization of European biotechnology industry to develop POC diagnostic tests
      - For early identification and differentiation of infectious disease-causing agents
  - To seek for novel molecular targets in pathogens and candidate drugs against them
- Strengthened Transatlantic cooperation
  - Transatlantic Taskforce on Antimicrobial Resistance (TATFAR since 2009)
Reduction of time for microbial detection and identification

“Need for speed”
Medical microbiology laboratory
Challenges in 2011

**Theranostic approach**

- Turnaround time
  - collection of specimen
- Identification
  - Relevant pathogens
- AST

Optimized management of patient and Infectious diseases

Specimen Analysis:

*Delayed results are unhelpful for clinicians!*
How could rapid bacterial identification improve the management of septic patients?

“... every hour without adequate treatment in septic shock is clearly associated with a 7.6% decrease in survival ...”

- **Severe sepsis and septic shock**
  - Major motivation to identify bacteria present in blood quickly
    - Tools exists for positive blood cultures (MALDI-TOF MS, PCR, microarray, ...) but far more rapid needed

- **Clinical impact of rapid ID even if not AST**
  - Clue towards primary site of infection and targeted investigation
  - Reduction of empirical broad-spectrum antibiotics to a more narrow pre-emptive therapy treatment
    - Based on usual susceptibility (or natural R) of pathogens
    - If *E. coli*: stopping vancomycin and macrolides whenever prescribed

Kumar et al, CCM 2006; Emonet et Schrenzel Expert Rev Anti Inf Ther 2011
Rapid identification of a pathogen

Prime importance for effective provision of care to patients with infections

- Includes
  - Use of rapid bedside diagnostic tests
    - Need to be backed up by conventional culture techniques (for AST)
  - Rapid reporting of results
  - Pre-emptive culturing !!
  - Molecular diagnostics
    - Bacteremia is different from DNAemia
    - Sometimes challenge to interpret
Non cultural approach & POCT
Technological evolution
Identification and MALDI-TOF MS (>2009)

- 20-years old technology
- Becomes the standard for ID
  - < Isolated colonies
  - < Positive blood cultures

- Bacteria, yeasts, fungi
- Results within a few minutes
- Results 24 hours prior to conventional methods
- Interface LIS
- Cost-effective
- Clinical and therapeutic impacts

C.Meex’s poster
Various mass spectrometry methods & application in clinical microbiology

- **MALDI-TOF MS** (Bruker; Shimadzu/bioMerieux)
  - Bacterial ID
  - More specific databases in development
    - Virulence and resistance markers
- **PCR-ESI-MS** (*Electro Spray Ionization*), Plex-ID
  - Directly from sample: DNA extraction
  - 4-6 hours
  - Semi-quantitative ID of all organisms present including virus
    - Syndromic panels of infection
  - Coupled with amplification by PCR, broad range of primers
  - High sensitivity
  - Detection of virulence or resistance genes
  - Results // to microarrays but faster
  - Still very expensive
Various emerging applications of sequence-specific DNA amplification

- PCR and Real-time PCR
  - Single or multiplex
  - Screening, detection and quantitative assays
- Loop-mediated isothermal AMPlification (LAMP)
  - Direct detection
  - Fast, sensitive, robust
    - Salmonella, C. difficile, group B streptococci, ...
- Broad-range 16S rDNA PCR followed by sequencing
  - Major milestone in diagnostic of infectious disease
    - Negative cultured bone and joint infections, endocarditis,
      Al Masalma et al., 2009; Fenollar and Raoult, 2007
Point of-care-test platforms for early diagnosis of infection

To provide an integrated solution addressing technological challenges

- For rapid detection of bacteria, mycobacteria, fungi, viruses, host markers and resistance to antimicrobial drugs
- To enhance clinical decision-making
- To improve quality of care and clinical outcomes
- To improve targeted therapy and reduce overuse

- Specific probes
- Novel methods of sample preparation
- Ultra-high sensitive detection methods

Results availability in less than 2 hours/30 min for IN/OUT patients
Point of-care-test platforms for early diagnosis of infection

Among EU funded projects

- RAPP-ID - Development of RApid Ppoint-of-Care ttest Pplatforms for Iinfectious Ddiseases
  - Bloodstream infections
  - Lower respiratory tract infections
  - Tuberculosis
  - From Be: UIA, KUL, RUG and Imec

- C4L - Chips for Life
  - Lower respiratory tract infections
  - From Be: CHU-Ulg, UIA and Coris

Huge challenges and synergies:
Biotechnologies, microtechnologies and clinical practice
Automation of culture process
Automation in bacteriology

Medical and economical plus values

- Labour shortages
- Increasing test volumes
- Reduction of TAT
- Reduction of laboratory errors associated with specimen handling
- Full traceability
- Improved workflow
- Enhanced quality

The ongoing challenge

Availability of high-throughput robots

- Gradually being introduced into everyday microbiology diagnostics
- Most cost effective use of resources

pm/ SBBC/ 15.10.2011
Automation in bacteriology
Medical and economical plus values
The ongoing challenge

Most cost effective use of resources

- Rational throughput if
- Large volume of specimens
- Often centralisation of services

- Danger of large-scale microbiology labs
- Logistics rather than diagnostics
- Risk of lost of clinical focus on the patient
First fields of automation and improvement: bloodcultures and mycobacteria

2011: 10th generation!!

- Sensitivity
- Flexibility
- Ergonomics
- Continuous measures
  - Earliness of detection
- Interface with LIS
- Evolution of culture broths
Since 2009

Plating and inoculation of specimens

**Systems**
- PREVI™ Isola, bioMérieux
- WASP, Copan
- INNOVA, BD
- InoculA, Kiestra
  - Semi-manual
  - Full-automated

**Characteristics**
- Media storage
- Types of specimen container
- Inoculation control
- Tips, swabs, volumes
- Plating method
- Streak patterns
- Traceability
- Biosecurity
- Sorting
- Interface with LIS
- Integration in a chain
- Slide module
- Output: plates/hour
PREVI™ Isola, bioMérieux

- Liquid specimen
- Tips
- 1 pattern: comb
- Max of 5 different media
- 180 plates/h
WASP, Copan
Slide module (option)

- Liquid specimens
- 1, 10 et 30 µl
- Max 9 media

The WASP manages all specimen types & styles
InoquIA, Kiestra
Semi- and Full-automated inoculation

- 6 – 30 media
- Barcode labelling at side dish
- Full Automatic ( decap / cap, pipet ) in plates, slides and tubes
- Shaking / vortexing
- Manual Interactive inoculation
- All specimen types
- Sorting + Stacking for incubators
- 300 – 500 inoculations per hour
Future: Total laboratory automation
Kiestra, Wasplab (Copan), bioMerieux concept

When the time to result is of the most importance
Reduce the time to results up to 2 days!
Transport
Incubation, digitized images of cultures

24H/24, 7J/7

Reading -/patient -/type of specimen -/...

Telebacteriology
Training – teaching
Verification, comparison
Archives
Medical microbiologist

To face the future
Medical microbiologist according to Union of European Medical Specialties (UEMS)

Main tasks

- Advice on diagnosis, treatment and prevention of infections
- Implementation of antibiotic policy
- Generation of surveillance data

To go to

- Integration of activities with Infectious Disease specialists to optimize the efficiency
Medical microbiologist in Europe

A specialty in many European countries

- Integrated training with Infectious disease
- Specialist’s mobility through Europe
- In Belgium
  - > 10.2012 – A 2-year certificate in "Infectious disease and clinical microbiology"
    - 25 modules
    - ULB, UCL and ULg
Mutations & a new culture are necessary to enjoy over the future of microbiology

KEY MESSAGE
- Improving time to result
  - Clinical impact only if used without any further delay by clinicians
- Non-culture approach and back-up cultures
  - Cost-effectiveness & clinical relevance still to show
- To develop and master technological advances
  - Laboratory automation and improved workflow
  - Avalanche of new methods for rapid diagnostics
- Increasing pressure for
  - Concentration, amalgation and outsourcing of lab service

Each laboratory should carefully think about how they can positively reorganize to speed up the diagnostics
A lot of opportunities to enjoy over the next few years!

Thank you