

Closer to the front door: clinical aspects of Microbiology automation


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Biography

- Background in paediatrics before training in Microbiology in Nottingham, UK
- NHS Consultant for 8 years in Nottingham and then Surrey, UK
- Frimley Health NHS Foundation Trust
 - Frimley Park Hospital & Heatherwood and Wexham Park Hospitals
- Surrey Pathology Services
 - Frimley Park Hospital, Royal Surrey County Hospital, Ashford & St Peters Hospitals



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Biography

- No specific affiliation to any private company or organisation
- Will not talk specifically about any product and presentation is not an endorsement of any specific product over another – make your own mind up...



Except this one...


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Aims & Objectives



- What is automation?
- What are the potential benefits of automation?
- Why does this matter?
- Automation in practice
- My model for the future infection diagnostics service

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What is automation?

- Automation - "The use or introduction of automatic equipment in a manufacturing or other process or facility"
- Automatic - "(of a device or process) working by itself with little or no direct human control"
- My definition - "anything that a device can do which makes delivery of service easier or more effective"
 - Let humans do what humans need to do and let machines and computers do the rest!


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Potential benefits

- Correct test done, on the correct sample, from the correct patient
- Improve accuracy of result (identification, antimicrobial sensitivities & clinical relevance)
- Reduce laboratory turnaround time
- Reduce mortality & morbidity
- Reduce length of stay
- Improve infection control
- Improve antimicrobial stewardship
- Improve user satisfaction – Patients & Clinicians

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Why do these matter?

- Correct test done, on the correct sample, from the correct patient
 - Common problems
 - Incorrect specimen type
 - Incorrect test requested for clinical scenario
 - Insufficient clinical information with request
 - Inadequate patient identifying information
- Solution
 - Pre-analytical automation of test requesting procedure



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Why do these matter?

- Improve accuracy of result (identification, antimicrobial sensitivities & clinical relevance)
 - Specific names of bacteria allow prediction of antimicrobial resistance patterns
 - Traditional laboratory methods can miss inducible antimicrobial resistance
 - Just because you find a microorganism doesn't mean you have to try and kill it!
- Solution
 - Identification (MaldiTOF, 16sRNA)
 - Sensitivities (reading of EUCAST, MIC methods)
 - Quantification & mixtures: Colonisation vs. Infection



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Why do these matter?

- Reduce laboratory turnaround time
 - Slow results damage reputation and reduce willingness of users to send samples
 - Impact on mortality & morbidity
 - Impact on length of stay
- Solutions
 - Screen for negative results as fast as possible
 - Reduce time taken to culture bacteria
 - Reduce time to detect non-culturable microorganisms



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Why do these matter?

- Reduce mortality & morbidity
 - For every hour delay in starting appropriate antimicrobials in sepsis mortality increases by 7.6%
 - Prolonged IV antimicrobial courses increase the risk of complications due to IV therapy e.g. CVC infections
- Solutions
 - Move the "laboratory" as close to the front door of the hospital as possible
 - Point of care diagnostics
 - Rapid identification of antimicrobial resistance



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Why do these matter?

- Reduce length of stay
 - Hospital capacity & winter pressures on bed stock
 - Increased patient turnover = increased financial return for hospital
 - Reduced risk of complications e.g. nosocomial infections
 - Patient satisfaction
- Solution
 - Reduce time to results which diagnose self-limiting infections or allow patients to convert to oral therapy or Outpatient Antimicrobial Therapy (OPAT)



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Why do these matter?

- Improve infection control
 - Delays in diagnosing communicable diseases or target organisms delays source isolation leading to increased risk of cross infection and outbreaks
- Solution
 - Point of care tests for communicable diseases or target organisms e.g. MRSA, C. difficile, Norovirus, Influenza etc.
 - Improve accuracy and reduce turnaround time of laboratory screening tests, particularly negative results
 - Detection of novel or specific resistance mechanisms e.g. carbapenemases



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Why do these matter?

- Improve antimicrobial stewardship
 - Right antibiotic at the right dose, route and duration, for the right infection at the right time to improve patient care whilst reducing antibiotic resistance
- Solution
 - Improved accuracy of sensitivity results
 - Faster sensitivity results allowing de-escalation or conversion to targeted antimicrobial therapy
 - Detection of inducible resistance
 - Expert rules





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Why do these matter?

- Improve user satisfaction – Patients & Clinicians


Fundamental aspect of the modern diagnostic laboratory



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What to automate?

Value		Volume of work	
		Low	High
Individual patient impact	Low	✗	✓✓
	High	✓	✓✓✓

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Low volume, high impact ✓

- Sample types
 - Blood cultures
 - Cerebrospinal fluids
 - Faeces – hospital onset diarrhoea (C. difficile)
- Predictive sensitivities by earlier identification
- Reduced mortality and length of stay
- Increased capture of communicable infections
- Reduced antibiotic burden by earlier change to targeted treatment

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Blood cultures ✓

- Pre-automation: 3-6 days
 - Automated incubator 1-2 days
 - Pure culture & identification 1-2 days (predicted sensitivity)
 - Sensitivities 1-2 days
- Post-automation: 1-2 days
 - Automated incubator 1-2 days
 - Pure culture & identification 4 hours (predicted sensitivity)
 - Sensitivities 1 day (possible 5-8 hours?)
- Future: < 1 day
 - POC incubator placement
 - Pre-incubation + identification direct from blood culture
 - Targeted multiplex PCR by clinical information

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Cerebrospinal fluids ✓

- Pre-automation: 2-10 days
 - Culture & sensitivity 2 days
 - Molecular detection 3-10 days
- Post-automation: 1-2 days
 - Culture & sensitivity 2 days
 - Molecular detection 1-2 days
- Future: < 1 day
 - Targeted multiplex PCR by clinical information

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Clostridium difficile ✓

- Pre-automation: 1-2 days
 - Cell culture plus confirmation by blocking
- Post-automation: 4-6 hours
 - GDH
 - Toxin assay
 - Lateral flow PCR
- Future: POC
 - Improved "card" techniques
 - Molecular "plug & play" technologies

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High volume, low impact ✓

- Sample types
 - Faeces
 - Sputum
 - Serology
- Increased capture of communicable infections
- Predictive sensitivities by earlier identification
- Reduced antibiotic burden by earlier change to targeted treatment
- Reduced length of stay

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Faeces ✓

- Pre-automation: 2-4 days
 - Culture 2 days
 - Sensitivities 2 days
- Post-automation: <1 day (+ 1 day)
 - Multiplex PCR
 - Targeted culture and sensitivity
- Future: POC
 - Improved "card" techniques
 - Molecular "plug & play" technologies

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Sputum ✓

- Pre-automation: 2-4 days
 - Culture 1-2 days
 - Identification and sensitivities 1-2 days
- Post-automation: 1-3 days
 - POC antigen testing for *S. pneumoniae* and *L. pneumophila*
 - Culture 1-2 days
 - Identification 1 day (predicted sensitivity)
 - Sensitivity 1 day
- Future:
 - Targeted multiplex PCR by clinical information

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Serology ✓

- Pre-automation: 1-7 days depending on arrival in lab
 - ELISA
 - CFTs
- Post-automation: 1-3 days
 - Twice weekly or more testing
 - Multi-test platforms
 - Syndromic testing by clinical information
- Future:
 - Limited value?
 - Targeted multiplex PCR by clinical information

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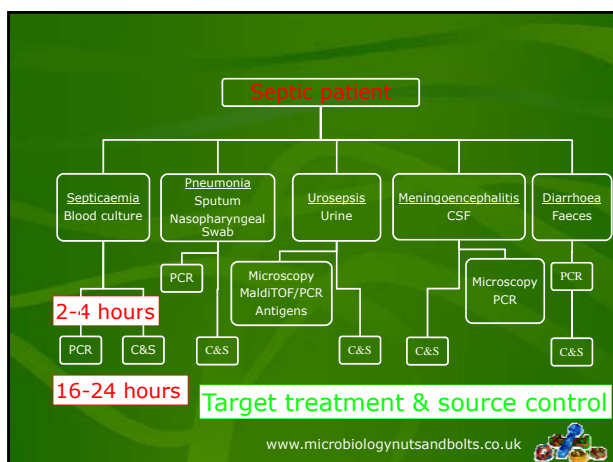


High volume, high impact ✓✓

- Sample types
 - Urines
 - Faeces – community onset diarrhoea
- Reduce use of antibiotics by allowing delayed treatment
- Increased capture of communicable infections
- Predictive sensitivities by earlier identification
- User satisfaction in primary care!

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Sepsis diagnoses

- **2-4 hours**
 - Pneumonia
 - S. pneumoniae
 - H. influenzae
 - S. aureus
 - L. pneumophila
 - K. pneumoniae
 - P. aeruginosa
 - Non-culturables
 - Viruses (Flu, RSV, etc)
 - Meningoencephalitis
 - S. pneumoniae
 - N. meningitidis
 - L. monocytogenes
 - H. influenzae
 - E. coli
 - S. agalactiae
 - Viral (HSV, Entero, etc)
 - Cryptococcus spp.
 - Urosepsis
 - AmpC
 - ESBL
 - CPE
- **16-24 hours**
 - Septicaemia
 - S. aureus (MRSA)
 - S. pneumoniae
 - S. pyogenes
 - S. agalactiae
 - L. monocytogenes
 - Enterococcus spp. (Van A/B)
 - N. meningitidis
 - H. influenzae
 - Enterobacteriaceae (KPC)
 - P. aeruginosa
 - A. baumannii
 - Candida spp.
 - Culture & sensitivity
 - Campylobacter spp.
 - Salmonella spp.
 - C. difficile
 - E. coli and Shigella spp.
 - E. coli O157

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Teenager with meningism

- **1 hour**
 - Blood cultures taken started on IV Ceftriaxone
 - Chest X-ray normal, no diarrhoea, urine dipstick negative
- **2 hours**
 - Lumbar puncture performed
- **4 hours**
 - Confirmed Meningococcal meningitis
 - Changed to IV Benzylpenicillin for 7 days
- **Benefits:** reduced complications, duration of antibiotics & length of stay

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Elderly lady with sepsis

- **1 hour**
 - Blood cultures taken started on IV Piptazobactam
 - Chest X-ray no consolidation, no diarrhoea, urine dipstick positive
- **2 hours**
 - Urine microscopy positive, ESBL positive E. coli detected by MalDI/TOF or PCR
 - Antibiotics escalated to IV Meropenem
- **16 hours**
 - Confirmed ESBL positive sepsis
- **Benefits:** reduced mortality

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Neonatal sepsis

- **1 hour**
 - Blood cultures taken started on IV Benzylpenicillin plus Gentamicin
 - Chest X-ray no consolidation
- **2 hours**
 - Lumbar puncture performed raised WBC
- **4 hours**
 - Confirmed L. monocytogenes meningitis
 - Changed to Ampicillin and Gentamicin for 3 weeks
- **Benefits:** reduced mortality & complications, public health follow-up

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The elephants in the room

- **Expensive**
 - Justify cost to lab against savings by users, reduced mortality, reduced length of stay or increased reputation?
- **Dependent on IT system**
 - Ultimately it doesn't matter how good your lab is if you can't receive and give out information
 - Multiple IT platforms in labs, wards and GP practices
- **Have to be able to recognise sepsis in order to use a sepsis pathway!**



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Recognising sepsis...



- The problem with managing septic patients is failing to recognise sepsis
- Surviving Sepsis Campaign
- The UK Sepsis Trust
- Should diagnostic companies be working with these organisations and promoting the recognition of sepsis?

1. Does the patient have a potential source of infection?

• Pneumonia	• Intracranial bleed/abscess
• Bacteremia	• Bone or joint infection
• UTI	• Wound infection
• Acute abdomen	• CNS infection
• Meningitis	• Other

2. Does the patient have any signs or symptoms of infection? **ANY** or more of the following:

• Temperature >38°C	• Respiratory >20/CPM
• Tachycardia >90bpm	• Tachypnoea >22bpm
• Leucopenia <4000/CL	• Leucocytosis >12000/CL
• Altered mental state	• Hyponatraemia <130mmol/L

3. Does the patient have evidence of organ dysfunction (measured by the following):

- Sepsis based process >4mmHg
- **OR** Mean arterial pressure <65mmHg
- Sepsis based process >4mmHg
- Bilateral pulmonary infiltrates
- **PLUS** P/FiO₂ <300 or SpO₂ <90%
- Bilateral pulmonary infiltrates
- **PLUS** PaO₂/FiO₂ ratio <300*
- BUNa >34mmol/L
- Creatinine >175umol/L
- **OR** urine output <0.5ml/kg/hour for more than 2 hours
- **OR** APTT >40 seconds
- Glasgow coma <15
- **OR** GCS <10
- Platelet count <100x10⁹/L
- Lactate >2mmol/L

*P/FiO₂ corrected for FiO₂ = (P/FiO₂) / (FiO₂ / 760) as % corrected and a normal e.g. 32% = 9.3


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Conclusions

- Get closer to the front door, the faster the result the better the outcome...?
- Potential benefits of automation include:
 - Correct test, correct sample, correct patient
 - Improve accuracy of result (identification, antimicrobial sensitivities & clinical relevance)
 - Reduce laboratory turnaround time
 - Reduce mortality, morbidity & length of stay
 - Improve infection control & antimicrobial stewardship
 - Improve user satisfaction – Patients & Clinicians
- Automation is expensive: cost needs to be offset against savings outside of the laboratory (not just financial!)


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Microbiology Nuts & Bolts

Further reading:


- Microbiology Nuts & Bolts by Dr David Garner
- www.microbiologynutsandbolts.co.uk
- Facebook page for Microbiology Nuts & Bolts





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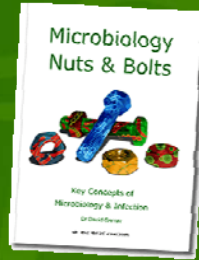



- Royal College of Pathologists**
 - A well-written book...concise, well set out and easy to use. It contains a wealth of useful information and is a valuable resource
- Royal College of Physicians**
 - This book delivers a uniquely relevant and accessible take on microbiology and does an excellent job of bridging the gap between the dry lists of pathogens learnt at medical school and the clinical reality of infection
- British Society for Antimicrobial Chemotherapy**
 - This book provides an impressively broad coverage of microbiology in theory and practice and I can see uses for it for students, junior doctors and general practitioners
- Royal Pharmaceutical Society**
 - Pocket guide to all things infection related packs a vast amount of information into a small space, and would be a useful back-up or portable revision aid for any pharmacist dealing with infection
- Institute of Biomedical Science**
 - A comprehensive yet concise book that would be useful to any healthcare professional managing patients with infections
- Hospital Infection Society**
 - A very good pocket guide covering the basics of microbiology... It forms a good base of knowledge for specialist trainees

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Any Questions?



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