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

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…

Questions: Blood cultures

- What is a blood culture?
- What has changed over the last 15 years?
- What is the purpose of a Microbiology Laboratory?
- Is there an argument for maintaining the *status quo* or should we be encouraging change?
- What are the benefits or risks of the status quo?
- What are the benefits or risks of change?
- Where might blood cultures fit into an "ideal network laboratory"?

What is a blood culture?

- The "gold standard" investigation for the detection of microorganisms in blood
- BUT UK SMI doesn't actually say what one is…
- Method used to detect bacteria or fungi in blood by growing the microorganism

What has changed over the last 15 years?

- Very little…!
- Still use essentially the same methods of collection, incubation and
- MaldiTOF
- Automated MIC testing e.g. Vitek
- 16s RNA PCR
- Loss of comparative Stokes method for sensitivity testing

How do we improve on the "gold standard"?

Purpose of a Laboratory

- Correct test done, on the correct sample, from the correct patient
- Speed: providing an accurate an informative result in a clinically meaningful time frame!
- Improve antimicrobial stewardship
- Improve user satisfaction – Patients & Clinicians

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The *Status Quo*

- For:
  - Familiarity with test
  - Cost neutral
  - It works; it is still the current "gold standard"
- Against
  - Change in how microbiology being delivered e.g. Networks
  - It's slow (24-48 hours?)
  - It no longer fits with clinical approaches to sepsis management?

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An argument for change

- Antimicrobial stewardship
  - Since 2005 antibiotic prescribing has increased by 30% (12% in hospitals) with an over-reliance on Beta-lactamase inhibitor combinations (40-50% reduction in cephalosporin and quinolone use over the same time period)
- Antimicrobial resistance
  - MRSA, VRE, ESBL, CPE…
- Infection control
  - Early identification of resistant microorganisms leads to early isolation of patients

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An argument for change

- Surviving sepsis
  - For every hour delay in starting appropriate antimicrobials in sepsis mortality increases by 7.6% up to ≈ 40% by 6 hours!
- Microbiology knowledge gaps
  - RCPath produced curriculum to try to combat the poor knowledge of doctors in relation to pathology specialties including microbiology

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Sepsis: the dilemma…

Adequate cover
Mortality & Morbidity

Toxicity
Resistance
Complications e.g. CDAD

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Broad spectrum antibiotics

Toxicity
Resistance
Complications e.g. CDAD

Adequate cover
Mortality & Morbidity

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Narrow spectrum antibiotics

Adequate cover
Mortality & Morbidity

Toxicity
Resistance
Complications e.g. CDAD

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Reality?

Toxicity
Resistance
Complications e.g. CDAD

Adequate cover
Mortality & Morbidity

and narrow down as soon as possible…

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Before narrowing down

- Need to know:
  - The diagnosis e.g. UTI, pneumonia, etc
  - Identification of causative microorganism
  - Antimicrobial sensitivity
  - Clinical information including drug allergies and interactions, etc.
- How does the National Blood Culture SMI impact this?

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Blood culture SMI

Pre-analytical	≤ 4 hours
Gram film	≤ 2 hours
Rapid Ag tests	≤ 2 hours
Identification	≤ 24 hours (automated) ≤ 24-48 hours (conventional)
Sensitivities	≤ 24 hours (automated) ≤ 24-48 hours (conventional)
Reports	Immediate Gram film ≤ 2 hours other results

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The challenges?

Pre-analytical	≤ 4 hours	Transport
Gram film	≤ 2 hours	Staffing
Rapid Ag tests	≤ 2 hours	Staffing
Identification	≤ 24 hours (automated) ≤ 24-48 hours (conventional)	Technology
Sensitivities	≤ 24 hours (automated) ≤ 24-48 hours (conventional)	Technology
Reports	Immediate Gram film ≤ 2 hours other results	Informatics

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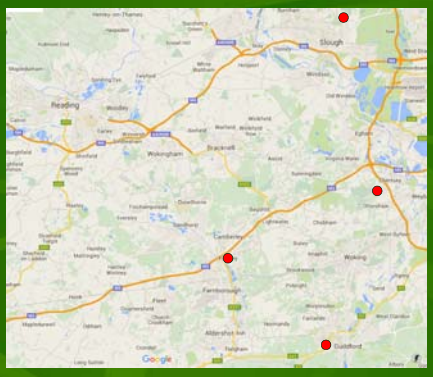

Google Maps

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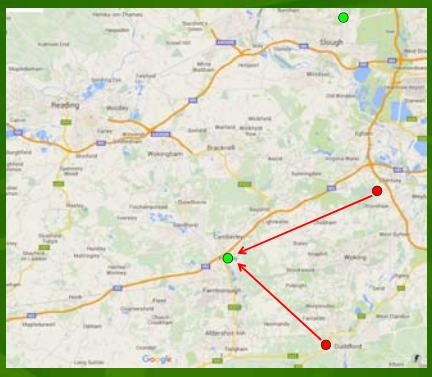

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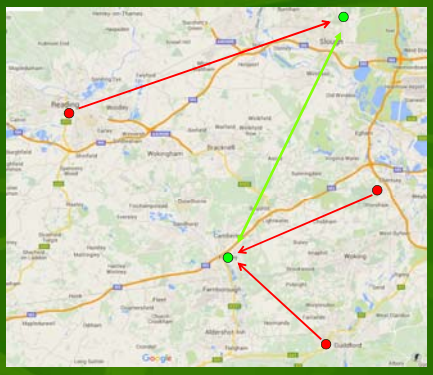

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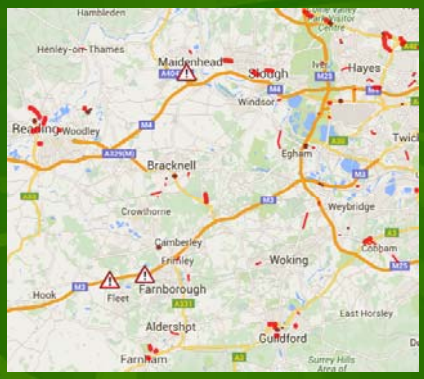

AA Roadwatch 12/11/2015

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The solutions?

- Point-of-care
- Creat "labs" in clinical areas
- "Hot labs" on each site for urgent samples
- Multidisciplinary areas in pathology with automated platforms and 24/7 staffing
- Link all platforms back to base laboratory
- Only move positive samples to the base laboratory that need further work
- Release negative samples at point of testing
- Consolidate specialist staff at base laboratory

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The ideal network laboratory in practice…?

Dear Santa, this year I'd really like…

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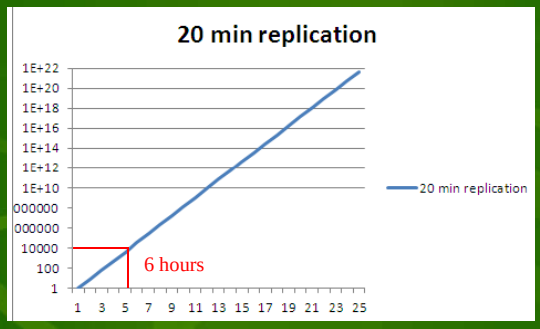
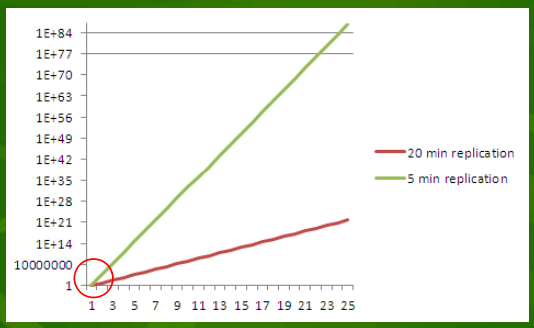
Ideal network laboratory…?

- Benefits
  - Fast turnaround time of negative results
  - Sepsis pathway
  - Only move samples that require culture or where transport is not the rate limiting factor for turnaround
  - POC blood cultures allows true negative turnaround e.g. 36 hours for neonatal units
  - Multi-discipline pathology MLAs run screening service on hospital site
  - 2 Central labs give emergency back-up if lab failure

Pushing the limits: Blood cultures

- What constitutes a positive blood culture?
- Does a blood culture have to signal positive to actually be positive?
  - Usually triggers at about 10^7/ml
- What are limitations of detection of other technologies applied to blood cultures?
  - MaldiTOF – 10^5/ml
  - 16sRNA PCR – 10^3-10^5ml
  - Target specific PCR – 10^3/ml





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 (or 6 hours?)
  - 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

Pan-laboratory automation

- Kiestra
  - 24/7 activity
  - Remote reading – laboratory, off-site, bedside?
  - Visual toolbox – automated reading and reporting of negative cultures
- Total lab automation
  - Combine platforms for various tests and use automation to move cultures between them
- Laboratory Information Management Systems
  - Rules based testing and auto-comments on reports
  - Expert rules to reduce time for reporting and authorising

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Technology driven sepsis pathway

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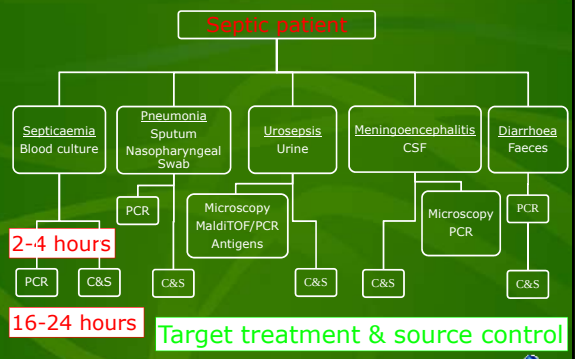

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Sepsis diagnoses

- 2-4 hours
  - Pneumonia
    - S. pneumoniae
    - H. influenzae
    - S. aureus
    - L. pneumophila
    - K. pneumoniae
    - P. aeruginosa
    - Non-culturables
    - Viruses (Flu, RSV, etc)
  - Urosepsis
    - AmpC
    - ESBL
    - CPE
  - Meningoencephalitis
    - S. pneumoniae
    - N. meningitidis
    - L. monocytogenes
    - H. influenzae
    - E. coli
    - S. agalactiae
    - Viral (HSV, Entero, etc)
    - Cryptococcus spp.
  - Diarrhoea
    - Campylobacter spp.
    - Salmonella spp.
    - C. difficile
    - E. coli and Shigella spp.
    - E. coli O157
- 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. baumanii
    - Candida spp.
  - Culture & sensitivity

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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 MaldiTOF 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?

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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

★★★★★

Available to buy on amazon.co.uk

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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
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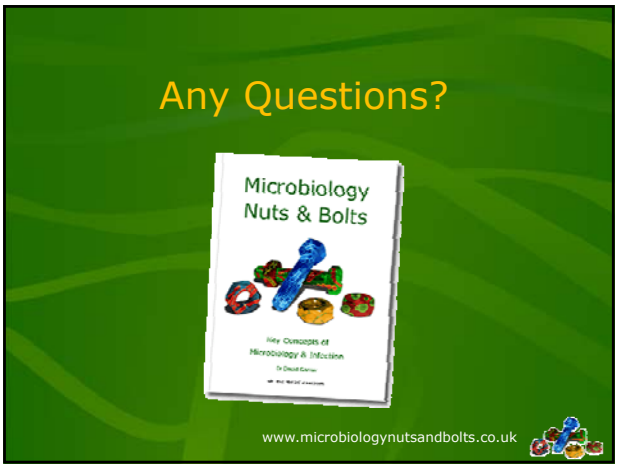
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