The role of the physician in laboratory medicine - a European perspective

Siraj Misbah
Consultant Clinical Immunologist
Oxford University Hospitals
Honorary Senior Clinical Lecturer in Immunology
University of Oxford

Chair, Immunology Division UEMS

Evolving role of medical doctors in laboratory medicine - an UEMS historical perspective

1962 - Section of Laboratory Medicine launched as umbrella body for all laboratory based specialties

Evolutionary forces

1988 - Section of Histopathology

2009 - Microbiology

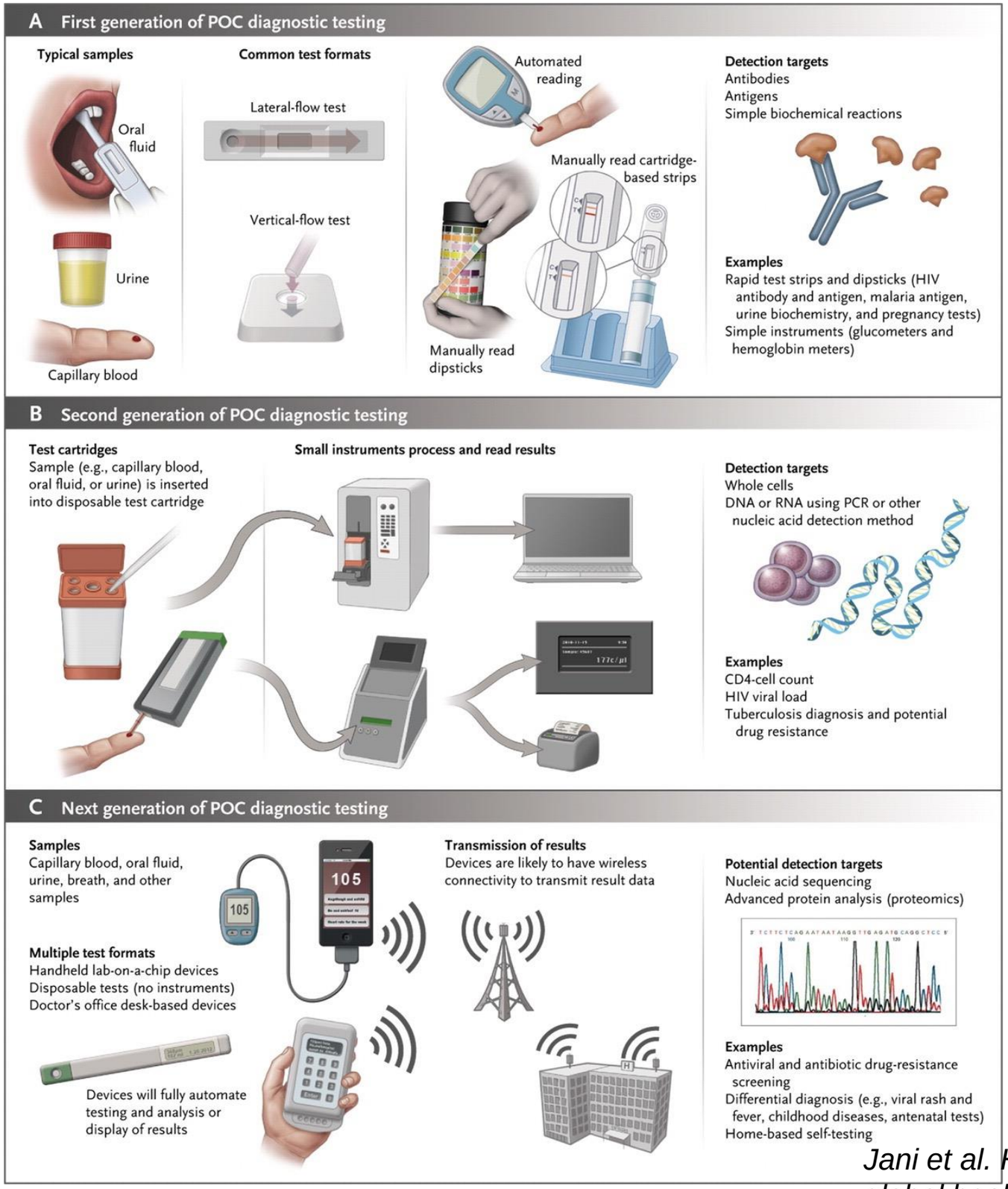
2015 - Clinical Chemistry, Immunology, Haematology -Transfusion Medicine, Polyvalent LM

The march of technology I - effect on the role of doctors in LM

- Generation of results from automated cross-disciplinary analysers not dependent on direct physician involvement

- Contrast with histopathology - role of the medical doctor in critical analysis of diseased tissue using a variety of conventional and molecular techniques has hitherto not been supplanted

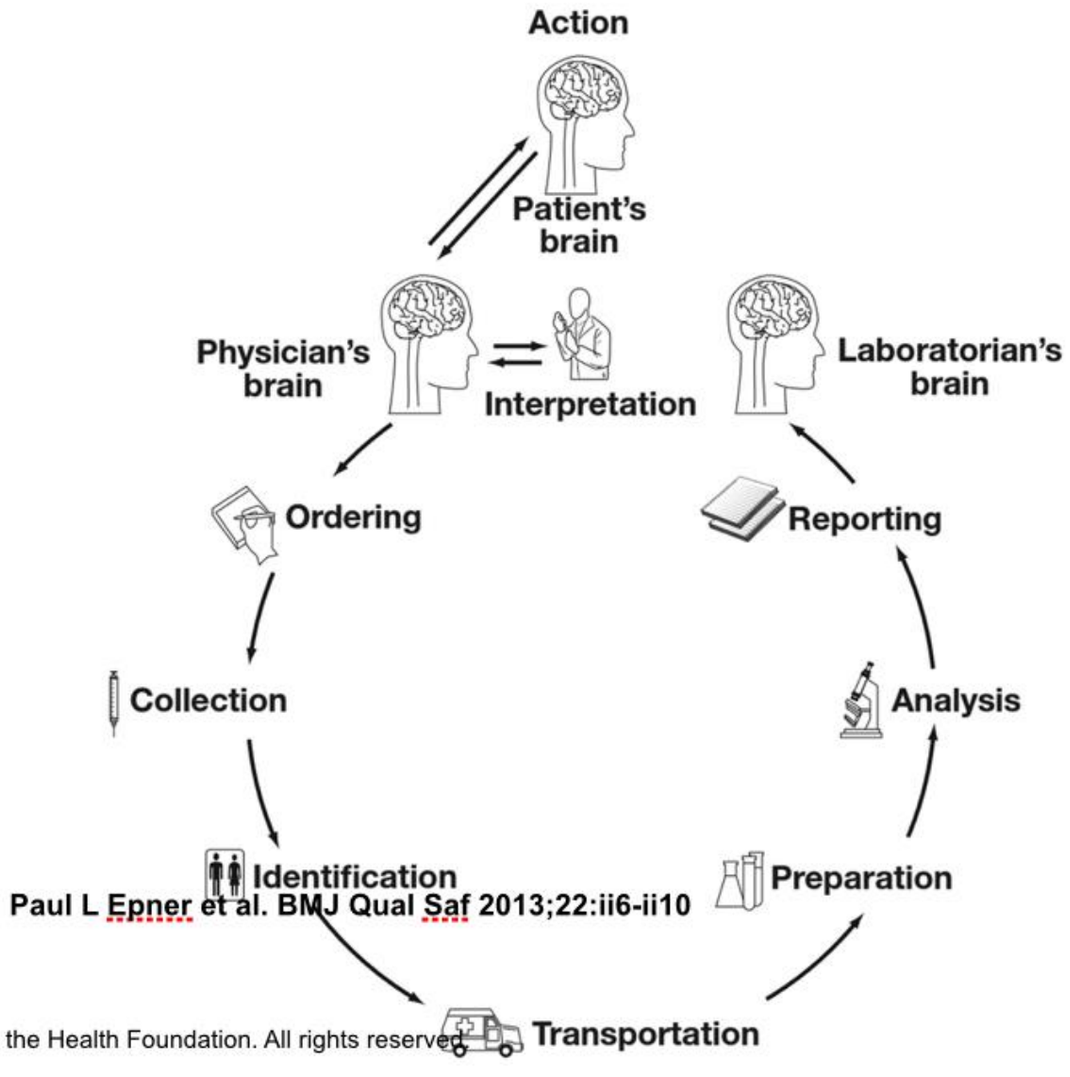
The march of technology II - effect of POCT on the role of doctors in LM



Jani et al. How POCT could drive innovation in global health NEJM 2013;368: 2319-2324

Physicians in laboratory medicine need to influence clinical outcomes

The 'Brain-to-Brain' loop, depicting the steps in the process of considering, performing and using laboratory tests for diagnosis.



Paul L Epner et al. BMJ Qual Saf 2013;22:ii6-ii10

BMJ Quality & Safety

Challenge

- How to demonstrate that physicians in LM influence clinical outcomes

when

- 70% of clinical decisions are said to be influenced by results of laboratory tests

Hallworth MJ.The ‘70% claim’: what is the evidence-base? Ann Clin Bioc hem 2011;48:487-8

Responsibilities of a laboratory-based physician

- Direction of clinical laboratories
- Provision of appropriate test repertoire
- Clinical liaison and interpretation of results
- Attendance at multi-disciplinary meetings
- Quality assurance
- Assay development and validation
- Defining the utility of existing and emerging biomarkers for disease diagnosis/monitoring/prognosis/screening,risk profiling,treatment monitoring and pharmacogenomics
- Clinical audit
- Demand management
- Education and training
- Hands on laboratory work (some disciplines)
- Co-ordinating direct patient care (in some disciplines) with test requesting, interpretation and reporting

Which of these responsibilities are truly physician-specific?

Adding value to laboratory medicine – concept of ‘SCIENCE’

Standardisation

Clinical effectiveness

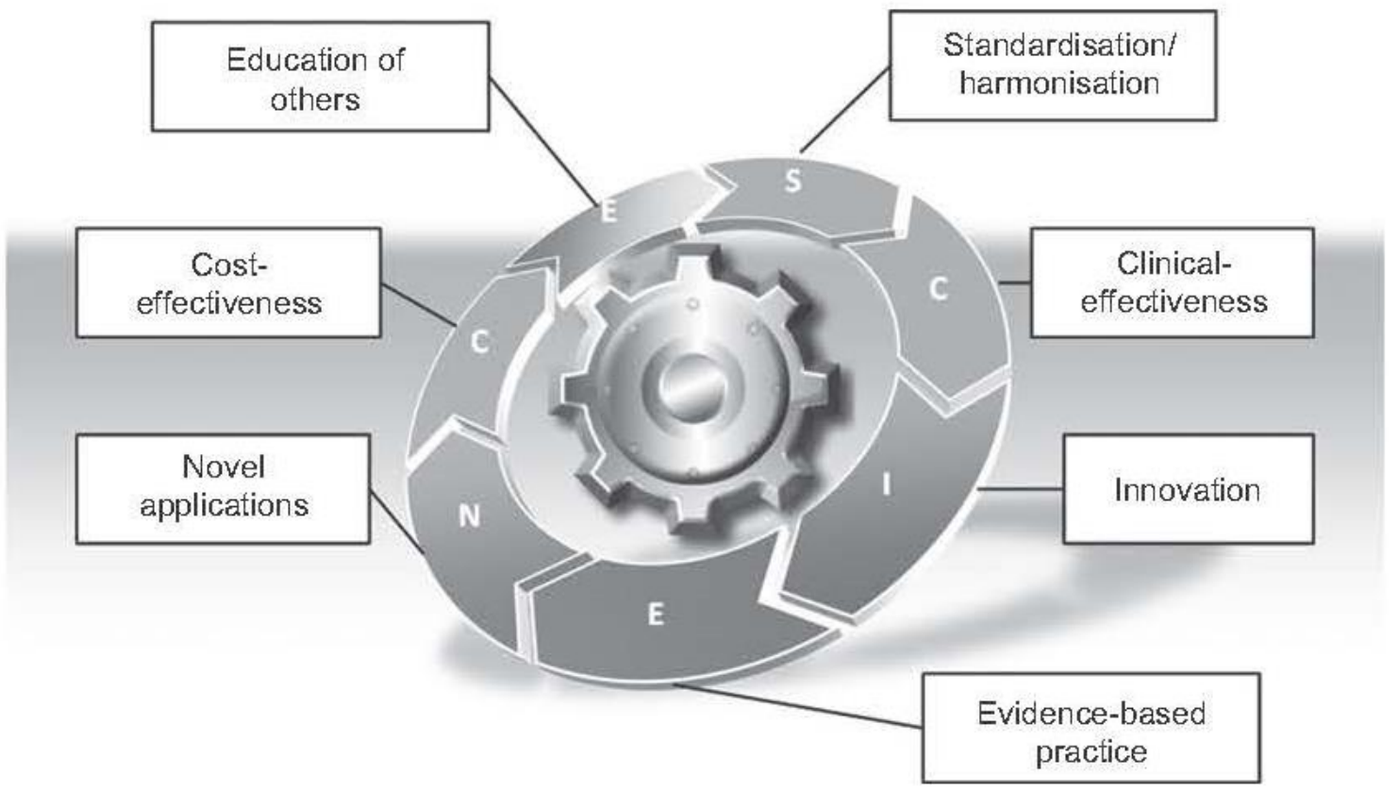
Innovation

Evidence-based practice

Novel applications

Cost-effectiveness

Education



Beastall G.Adding value to laboratory medicine:a professional responsibility. Clin Chem Lab Med 2013

Defining quality in clinical laboratories - are physician-specific metrics included?

- Extremely challenging - therefore none have been included in recognised quality programs such as the College of American Pathologists Q probe/track initiatives

  - Clinical quality indicators for laboratory medicine as defined by an expert panel of primary and secondary care physicians include communication of critical results, education of users and QA but did not include quality of interpretative comments

- Attempts at assessing quality of interpretative comments in biochemistry -

- Significant minority of comments felt to be inappropriate,misleading or in a few cases,dangerous

- No systematic objective evidence that provision of interpretative comments positively influences patient care or clinical outcomes

Nakhleh et al Arch Pathol Lab Med 2014;Lim et al Clin Chem 2004; Barth JH. Ann Clin Biochem 2012

Influencing clinical outcomes - a qualitative approach based on expert interpretation of results by a laboratory-based physician

- Concept illustrated by discipline-specific clinical case histories

- Cases highlight the clinical value of pro-active interventions by laboratory-based physicians by ensuring accurate diagnosis,providing guidance on appropriate treatment and avoidance of inappropriate interventions

Misbah et al J Clin Path 2013

Illustrative cases - I

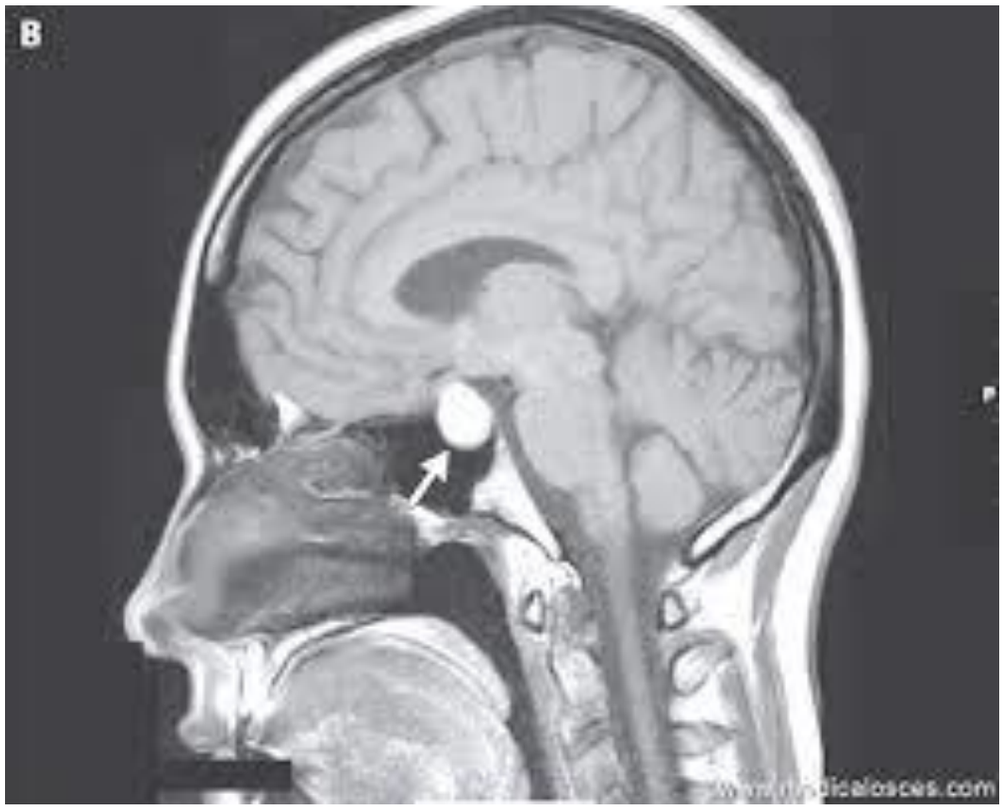
- Biochemistry - peri-menopausal woman with menopausal symptoms with plasma LH < 0.1 IU/L (ref range > 30),FSH 0.6 (ref range > 30).Inappropriately low LH/FSH prompts lab physician to raise the possibility of pituitary disease.

- Additional investigations instigated by laboratory reveals elevated prolactin at 6.1 IU/L (ref range 0.09-0.52)

- Review of history - chronic galactorrhea

- Cranial MRI - large pituitary tumour

- Lesson - correct interpretation of the significance of an unusually suppressed FSH/LH in a peri-menopausal woman by a lab-based physician and instigation of additional tests leads to diagnosis of pituitary tumour



Illustrative cases - II - Immunology

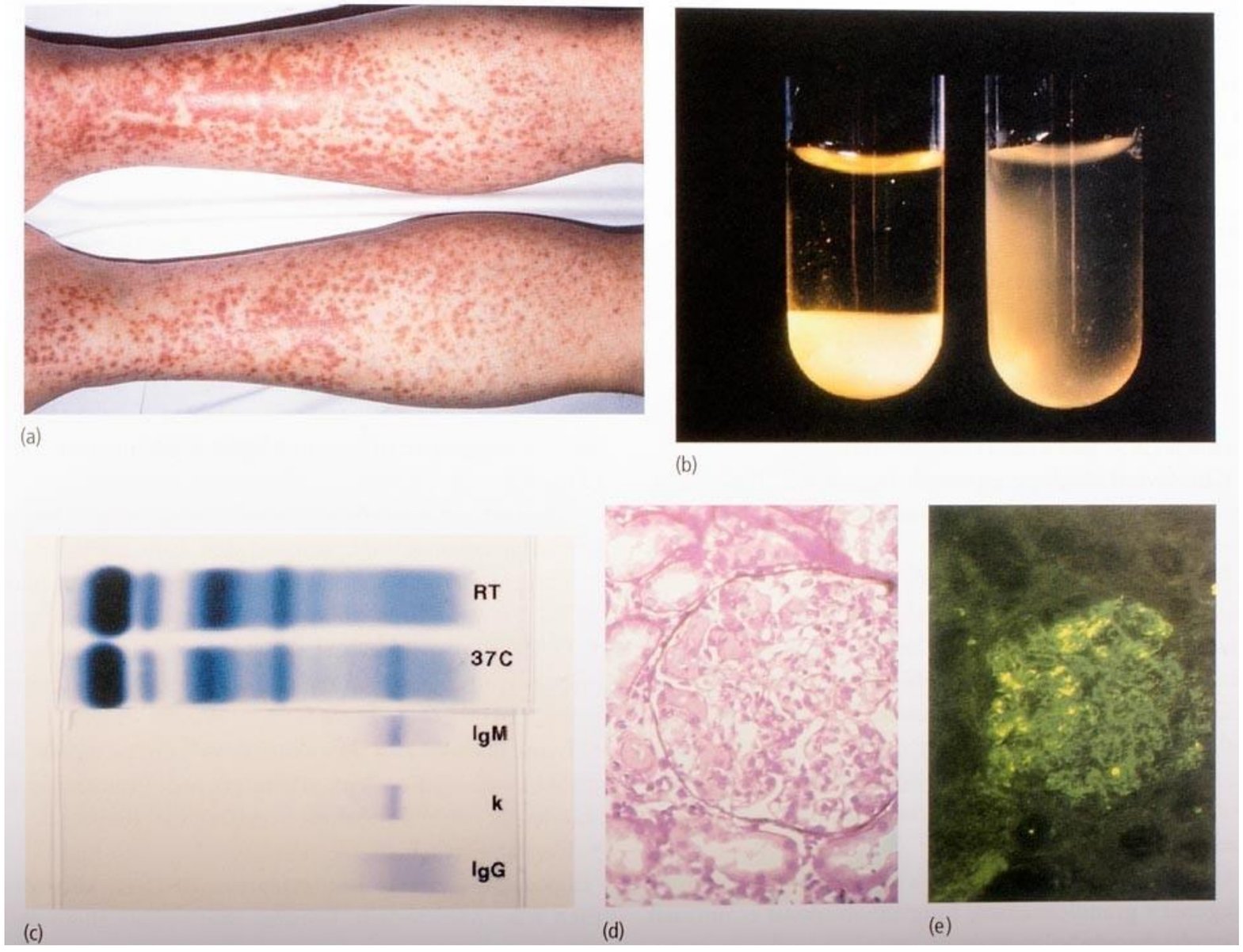


Fig – Medical Masterclass 2nd edition 2008,RCP London

- Adult female with arthralgia and purpuric rash
- Results of initial tests - ANA 1/160; Rheumatoid factor 180 IU/L (ref range < 40)
- No evidence of Rheumatoid arthritis on clinical assessment
- Results of further tests - anti-DNA,anti-ENA neg, C3 1.2 g/l (0.6-1.8),C4 0.02 (0.15-0.4)
- Combination of a strongly positive RF and low C4 led to the lab-based clinical immunologist raising the possibility of mixed cryoglobulinaemic vasculitis
- Lesson - correct diagnosis of Hepatitis C-associated cryoglobulinaemic vasculitis was a direct result of proactive clinical interpretative comments

Illustrative cases - III - Microbiology

- 22 yr old male with 3 month history of cervical lymphadenopathy,mild hepato-splenomegaly,malaise,night sweats and weight loss
- Results of tests requested by primary care physician: EBV,CMV serology consistent with past infection
- Haematology opinion requested because of concern of lymphoma
- Given the clinical history,laboratory physician requests toxoplasma serology:IgM and IgG strongly positive
- Lesson - Recognition of possibility and instigation of tests for toxoplasmosis by microbiologist leads to correct diagnosis and avoidance of biopsy

Illustrative cases IV - Haematology

- Adult female undergoing renal transplantation for chronic renal failure;peri-operative thromboprophylaxis undertaken with unfractionated heparin

- Operative procedure uneventful but post-operative period complicated by fall in platelet count from 220 to 80.

- Diagnosis of heparin-induced thrombocytopenia (HIT) suggested by haematologist at MDT meeting

- Testing for heparin-platelet factor4 complexes initiated by lab-based haematologist

- Change to alternative anti-thrombotic treatment recommended

- Lesson - failure to diagnose HIT by transplant team and consequent delay in stopping heparin are key learning points. Had the diagnosis of HIT not been made by the laboratory haematologist, it is likely that heparin would have been continued at a higher dose due to the mistaken assumption of inadequate anti-coagulation in the face of multiple thromboses

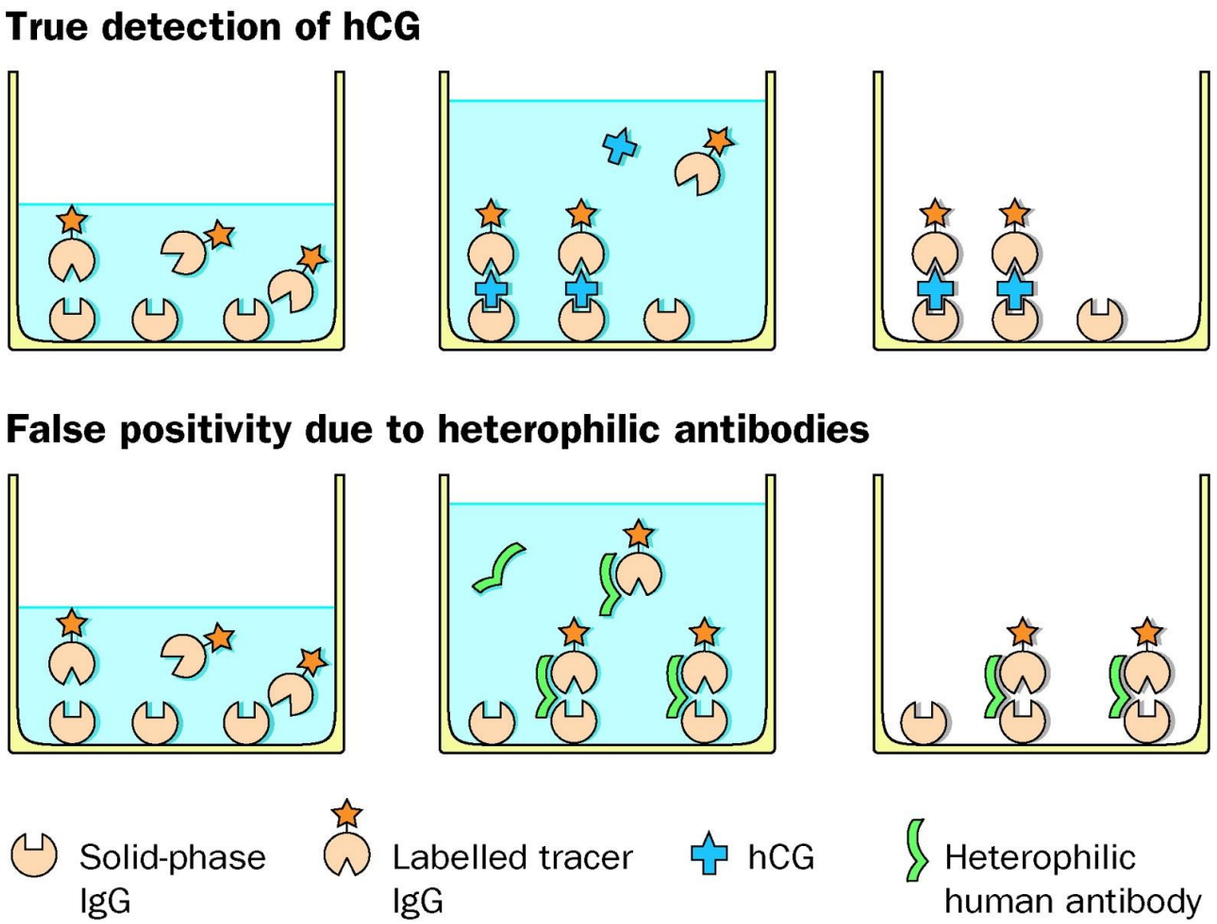
Influencing clinical outcomes - a qualitative approach based on expert interpretation of results by a laboratory-based physician – does this constitute hard evidence?

- Collection of anecdotal case histories does not constitute definitive evidence of the value of a laboratory-based physician
- Would a specialist physician or appropriately trained clinical scientist have made the same diagnoses?

Unsworth DJ,Lock RJ.Consultant leaders and delivery of hi gh quality pathology services (editorial). J Clin Path 2013

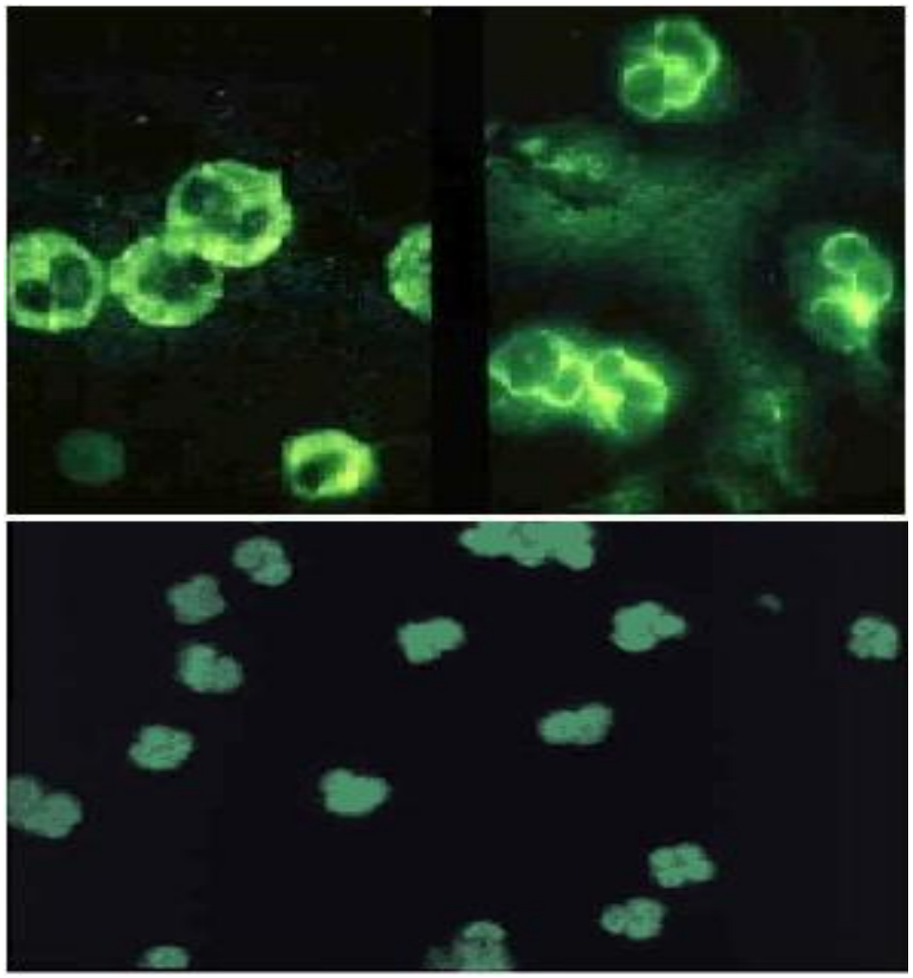
Influencing clinical outcomes through prevention of medical errors - need for informed clinical interpretation of test results I

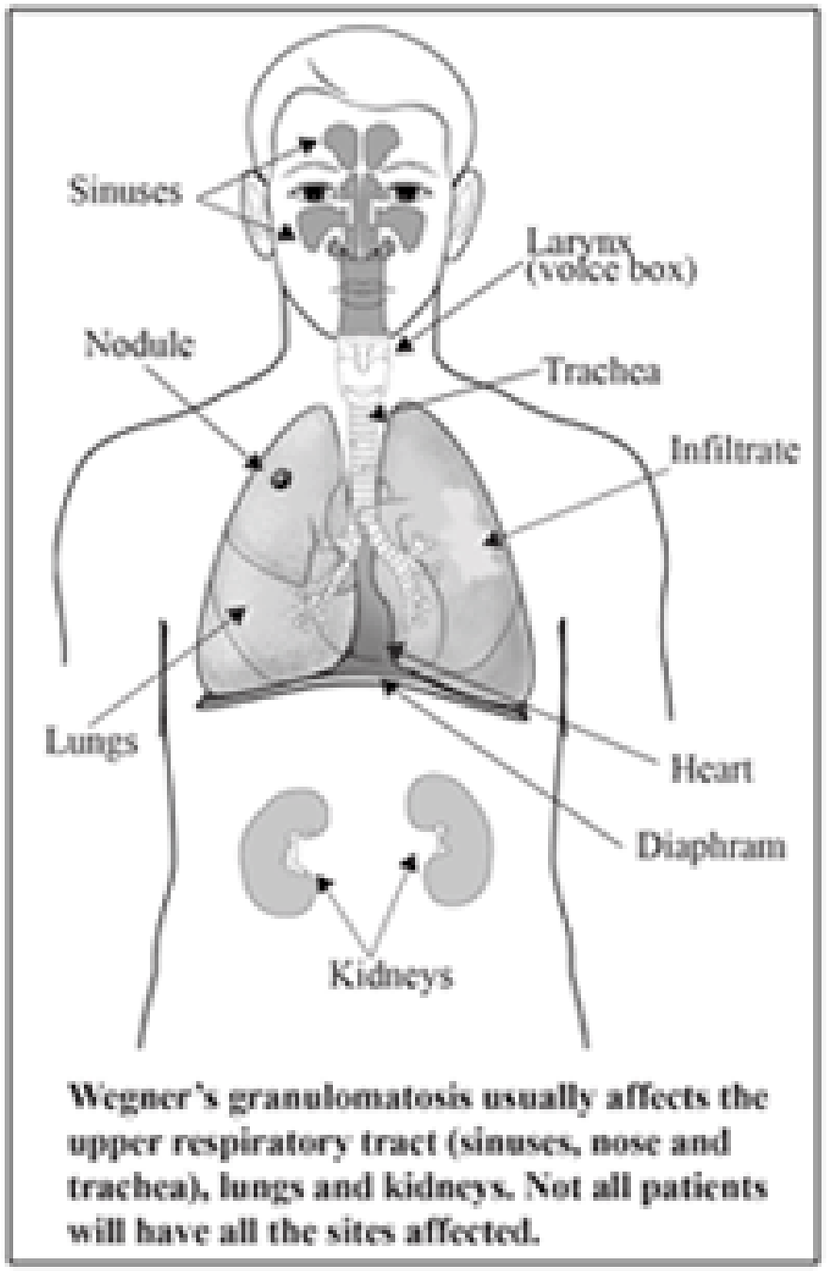
- Inappropiate clinical decisions as a result of erroneous test results generated through interference by heterophilic antibodies in immunoassays
- Example of spuriously elevated serum HCG - disastrous effects of misinterpretation
- Needless treatment of young women for ‘occult’ trophoblastic disease with chemotherapy and surgery



- *Rotmensch et al Lancet 2000;355:712-5*

Influencing clinical outcomes through clinical audit and demand management – example of ANCA as a marker of small vessel vasculitis





Wegner's granulomatosis usually affects the upper respiratory tract (sinuses, nose and trachea), lungs and kidneys. Not all patients will have all the sites affected.

Use of a gating policy to ensure rational ANCA testing – Oxford experience *(Arnold et al J Clin Path 2010)*

- Aim – to ensure that testing for ANCA is targeted at those patients with the highest pre-test probability of vasculitis

- When a request for ANCA was declined, requesting clinician is invited to contact laboratory if ANCA was still required.

Selection criteria for current gating policy – ANCA testing confined to these groups of patients:

- ***Chronic necrotising large airways disease***
- ***Cavitating pulmonary nodules***
- ***Suspected Churg–Strauss syndrome***
- ***Subglottic stenosis***
- ***Pulmonary–renal syndrome***
- ***Rapidly progressive glomerulonephritis***
- ***Cutaneous vasculitis accompanied by systemic symptoms***
- ***Mononeuritis multiplex***

Audit of clinical outcomes in 263 patients in whom ANCA testing was declined

- Duration of audit – 8 month period in 2007/08.
- Patients notes reviewed at a median of 154 days (IQR 118 – 190) of date of ANCA request.
- Final diagnoses :

HSP - 2%

RA, SLE, MCTD – 6%

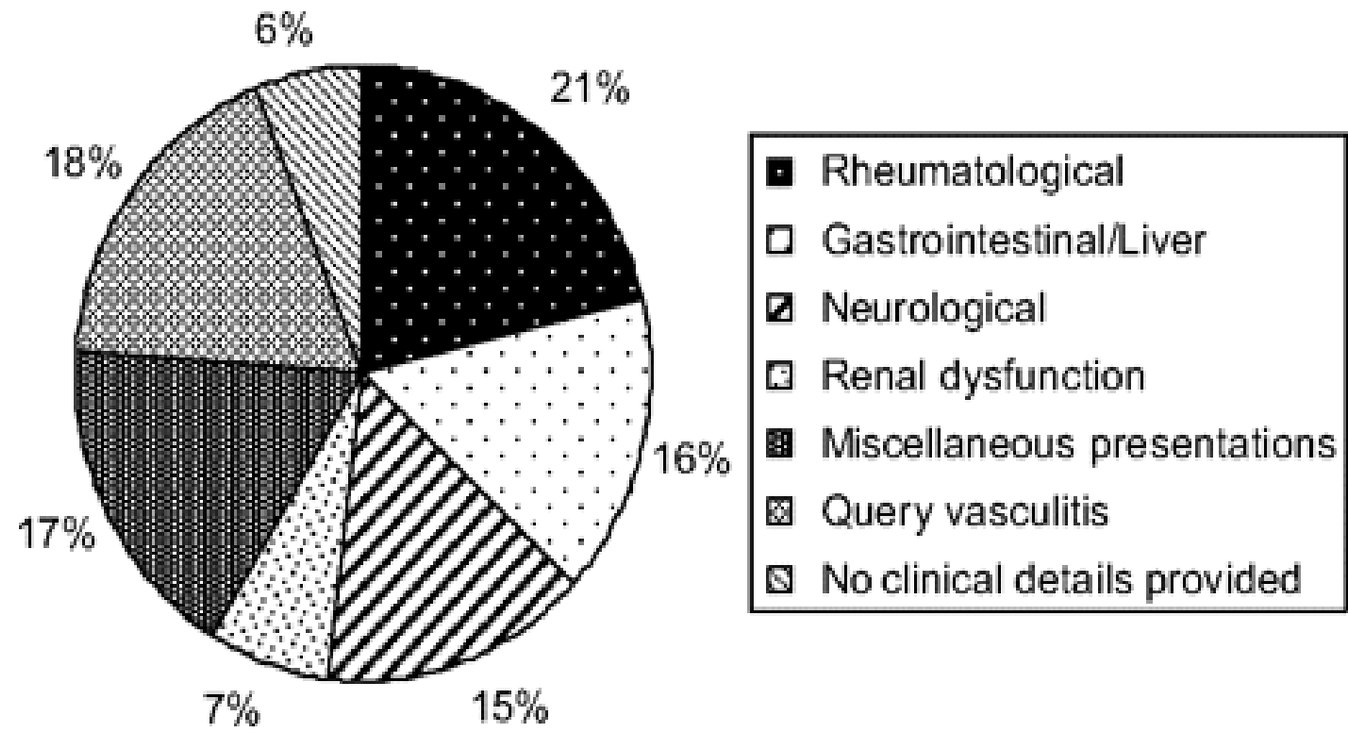
IBD, Liver disease – 11%

Non-vasculitic neurological disease - 14%

Non-vasculitic renal disease – 6%

Miscellaneous conditions – 49%

No diagnosis – 11%



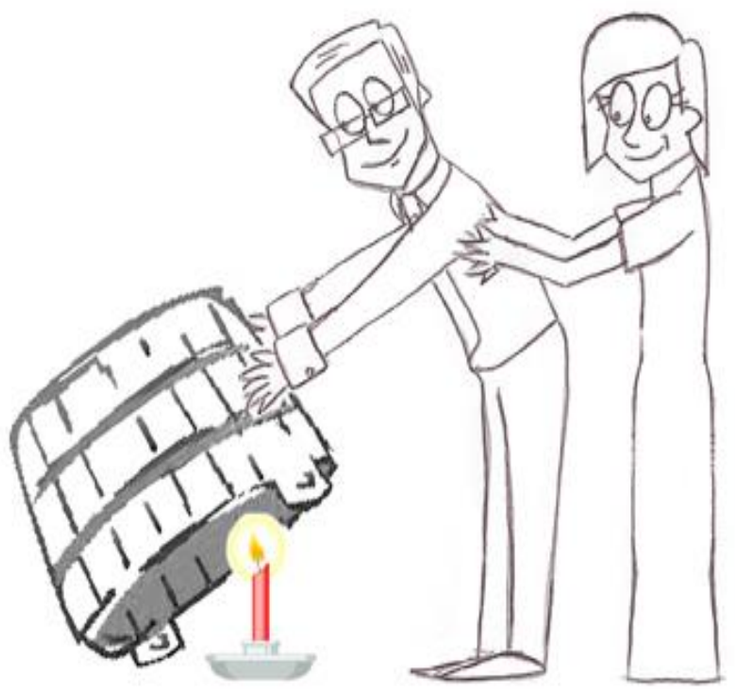
At 6 mth follow-up, no diagnoses of small vessel vasculitis of the WG-MPA spectrum

Challenge from healthcare commissioners

Assertion : A results-only service is perfectly adequate because clinicians are capable of interpreting test results

How should laboratory physicians respond?

Demonstrate continuing need for physicians in laboratories



"Don't hide your light under a bushel!"

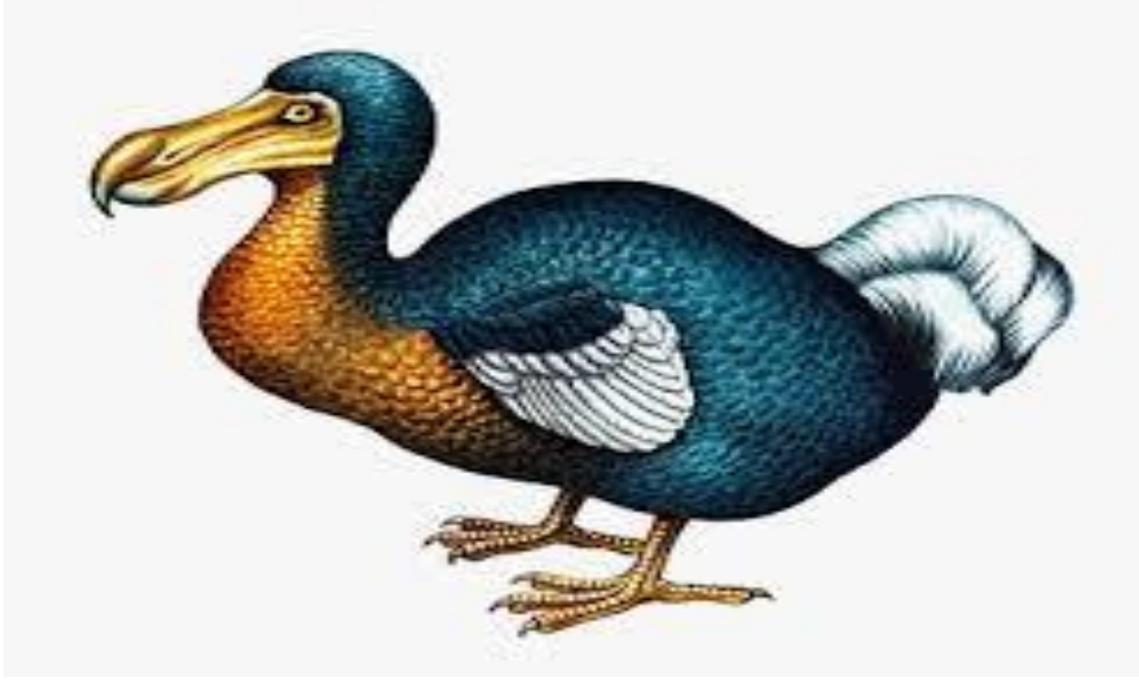
•Be seen and heard – on the wards, clinical meetings, grand rounds

•Peer credibility and support from requesting clinicians essential – getting colleagues to sing your praises has greater impact

• Bottom line : "The ……medical laboratory director must demonstrate value that translates into improved patient care, more efficient delivery of care, and increased revenue"

Thomson RB,Doern GV.What will the role of the Clinical Microbiology Laboratory Director Be in 2015? J Clin Micro 2011

Fate of the laboratory physician in 2050?



- Still required but will need to adapt to avoid being overtaken by evolutionary forces