SEVERE RESPIRATORY INFECTIONS IN THE ICU

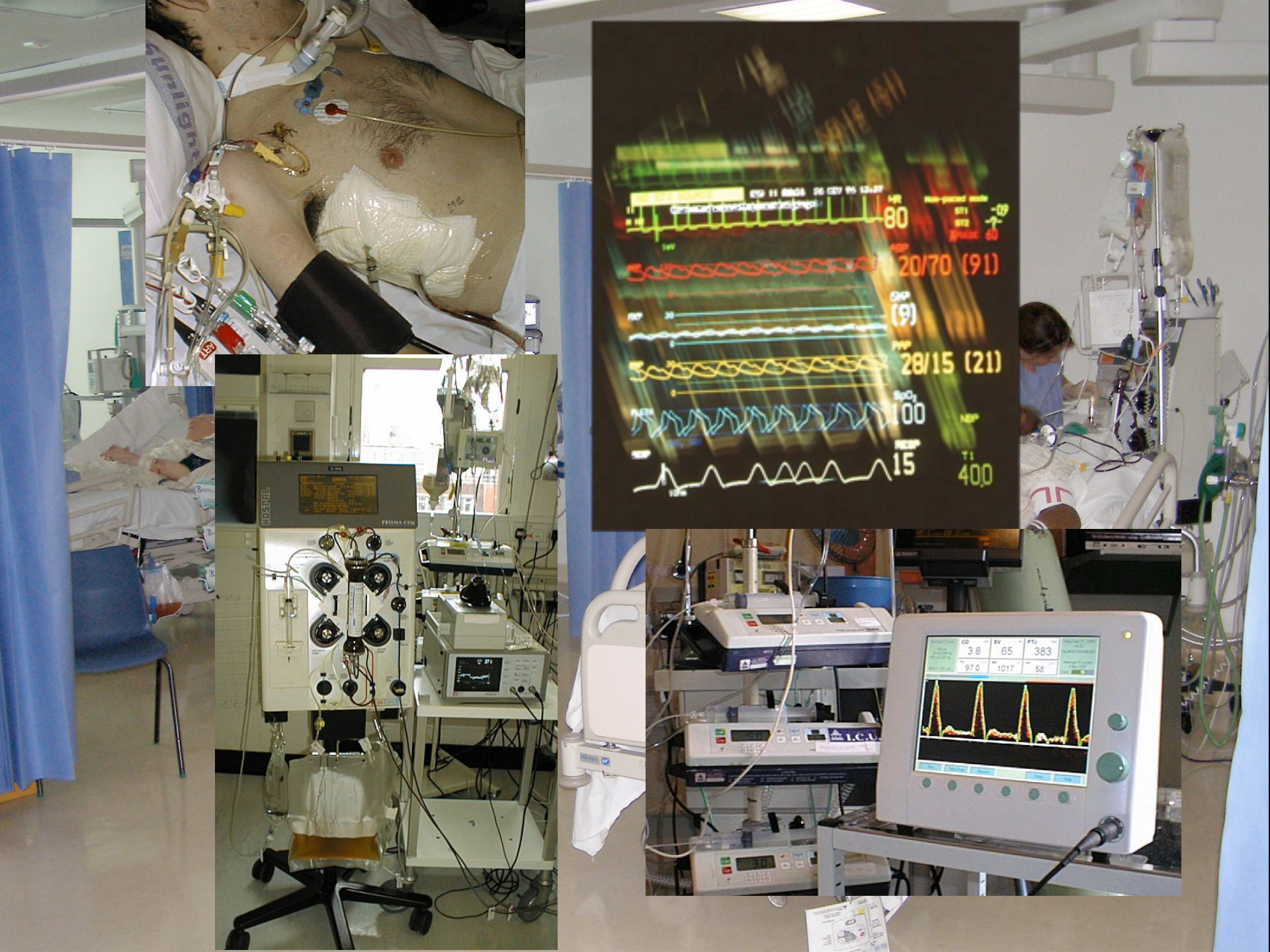
THE BLOOMSBURY INSTITUTE OF INTENSIVE CARE MEDICINE

UCL

MERVYN SINGER

BLOOMSBURY INSTITUTE OF INTENSIVE CARE MEDICINE

UNIVERSITY COLLEGE LONDON, UK


80
20/70 (91)
(9)
28/15 (21)
100
15
400
HOSPAL
PRISMA CFM
I.C.U.

INFECTION

CAP/HAP/VAP

PNEUMONIA

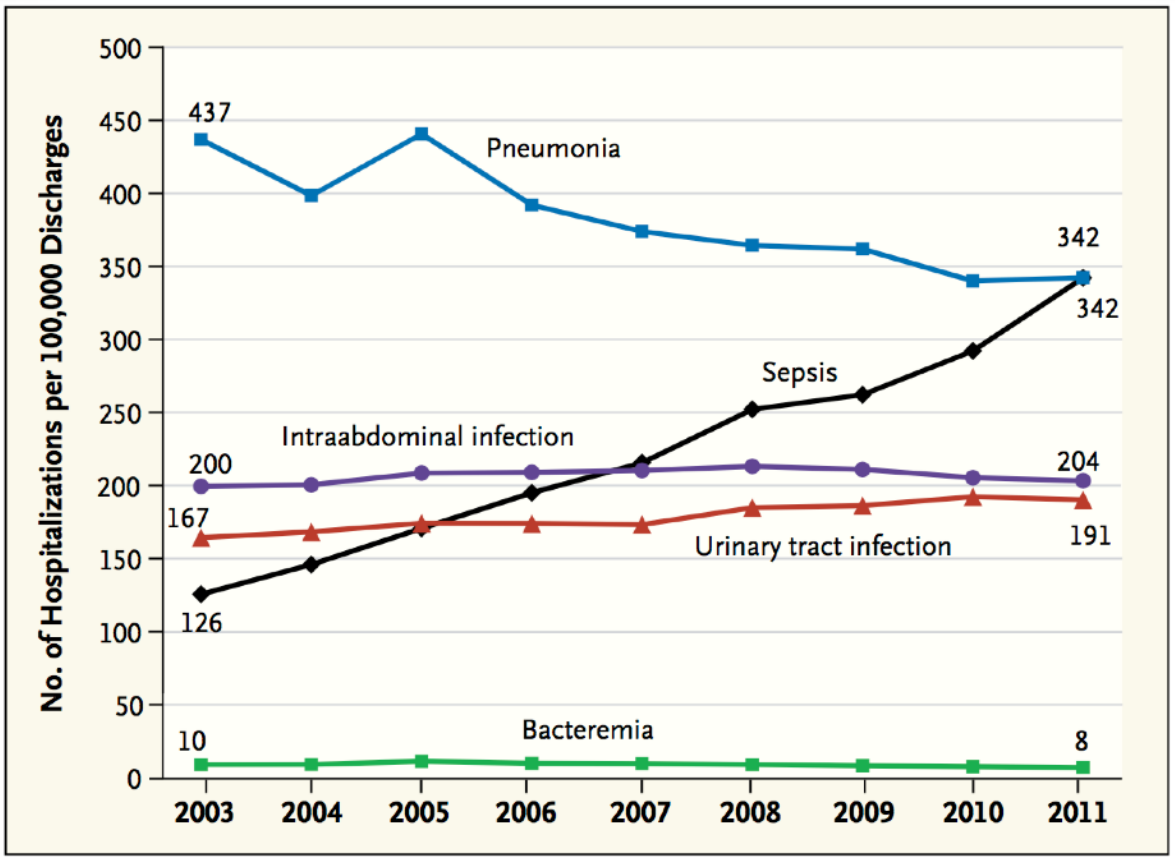
SEVERE SEPSIS

SEPSIS

SEPTICAEMIA

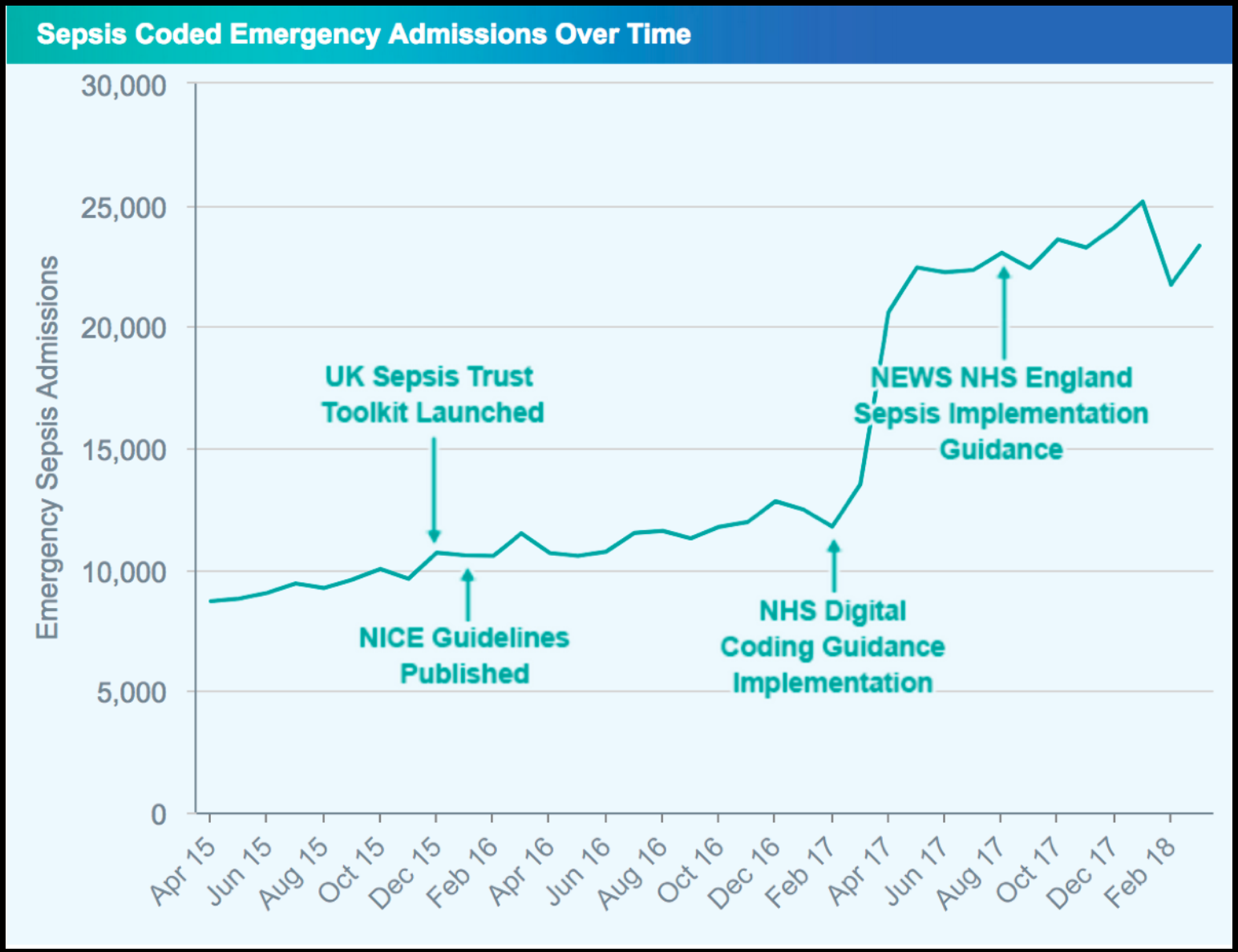
Regulatory Mandates for Sepsis Care — Reasons for Caution

Chanu Rhee, M.D., Shruti Gohil, M.D., M.P.H., and Michael Klompas, M.D., M.P.H.



Hospitalizations for Which Certain Infection Codes Were Listed as a Primary Diagnosis, 2003–2011.

NHS ENGLAND SEPSIS DASHBOARD



Primary diagnosis of Pneumonia; base HRG groups to:

Code Type	Code	Code Description	HRG 1
ICD	J189	Pneumonia, unspecified	DZ11

HRG code	HRG name	Non-elective spell tariff (£)
DZ11K	Lobar, Atypical or Viral Pneumonia, with Multiple Interventions, with CC Score 14+	7,866
DZ11L	Lobar, Atypical or Viral Pneumonia, with Multiple Interventions, with CC Score 9-13	6,473

Primary diagnosis of Sepsis; base HRG groups to:

Code Type	Code	Code Description	HRG 1
ICD	A419	Sepsis, unspecified	WJ06

HRG code	HRG name	Non-elective spell tariff (£)
WJ06A	Sepsis with Multiple Interventions, with CC Score 9+	10,625

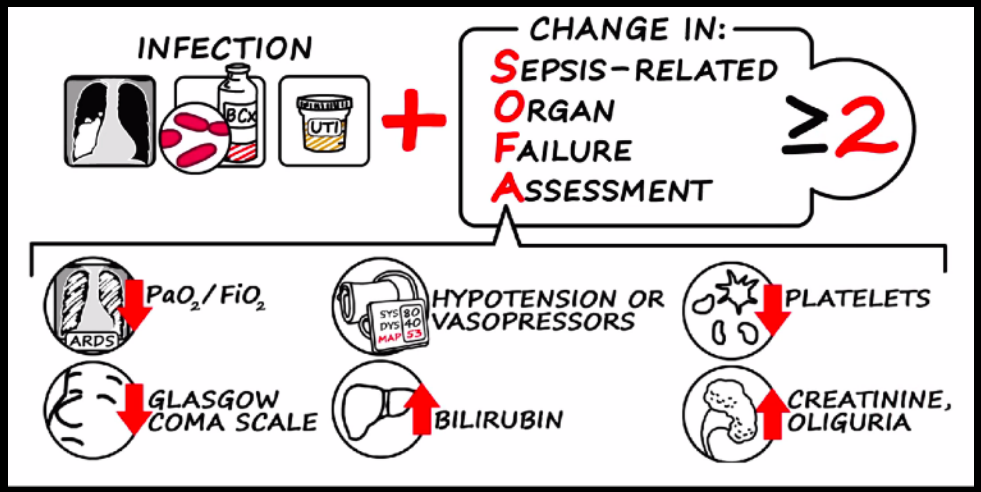
SEPSIS-3

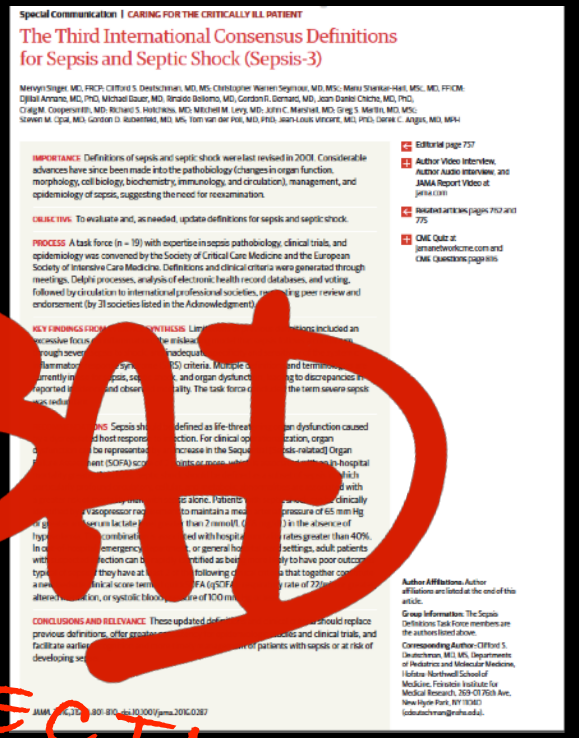
DEFINITION

sepsis = life-threatening organ dysfunction due

to a dysregulated host response to infection

CLINICAL CRITERIA




Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

BAD INFECTION

= ≥10% RISK OF DYING

JAMA. 2016;315(8):801-810.

SOFA SCORE

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

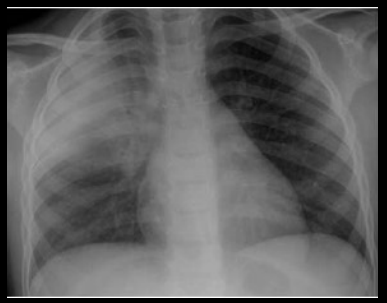
System	Score 0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.



Mortality <1%

Chest infection

ARDS (acute respiratory distress syndrome)

= host response to insult with

- outpouring of fluid + white cells into lungs
- fibrosis

Mortality 10-60%

Respiratory failure

(hypoxaemia and/or hypercapnoea)

Full ventilatory support

Oxygen ± non-invasive ventilation

Mortality <5%

CHALLENGES, DIAGNOSTIC CONUNDRUMS, ETC..

- community vs. hospital (± ventilator)-acquired
- previously healthy vs. immunosuppressed
- limited recognition of underlying pathogen - bacterial, viral, fungal …
- pathogen vs commensal?
- confounding acute and/or chronic pathologies/comorbidities/Rx
  - e.g. chest trauma, ARDS, lung fibrosis, complications of chemoRx
- treatment uncertainties - mono- or combination Rx, duration, adjuvant therapy (e.g. steroids)
- current and novel diagnostics

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INFECTING BUG VARIES BY LOCATION, PATIENT ...

- Community-acquired
  - In healthy patient, most likely to be:
    - Gram +tive, n.b. *pneumococcal*
    - Viral - usually seasonal .. ± 2° bacterial infection (staph, strep…)
  - In patient with underlying pathology/comorbidity, also think:
    - Colonisation —> infection (e.g P*seudomonas* in cystic fibrosis, *Haemophilus* in COPD)
    - Reactivation (*TB*)
  - Atypicals very rare in healthy population - *legionella, mycoplasma*..
  - Unusual pathogens (e.g. *Pneumocystis jirovecii, CMV,* fungal, *TB*) with endogenous (e.g. HIV) or therapeutic immunosuppression

INFECTING BUG VARIES BY LOCATION, PATIENT ...

- Hospital- (or ventilator) acquired
  - Often relates to transmission of local pathogenic flora (mainly by cough/droplet spread) or endogenous (from oropharyngeal/gut)
  - Bacteria - when found - predominantly Gram -tive
  - Organism and sensitivity pattern often follow local pattern
  - In immunosuppressed patient (chemo- or transplant Rx, long-term ICU patient..) think Gram -ve (Gram +ve less common) .. but also fungal, CMV, EBV, *Pneumocystis jirovecii*..
  - Viral - rarely looked for outside chemoRx patients

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DIAGNOSTIC CHALLENGES

- Causative organism infrequently identified
- 30-50% yield (blood, sputum, BAL) - why so low?
  - inadequate identification of pathogen (especially if on antibiotics or difficult to grow)
  - not due to bacteria (1/3 of community infections thought to be viral)
  - not due to infection
- False positives - commensals … low level multi-organism, or even high-level mono-organism growth .. yet WBC activation not looked for
- Long delay (days) before identification of organism/sensitivity patterns
- Molecular techniques underused in UK (cost, staffing…)

CHALLENGES, DIAGNOSTIC CONUNDRUMS, ETC..

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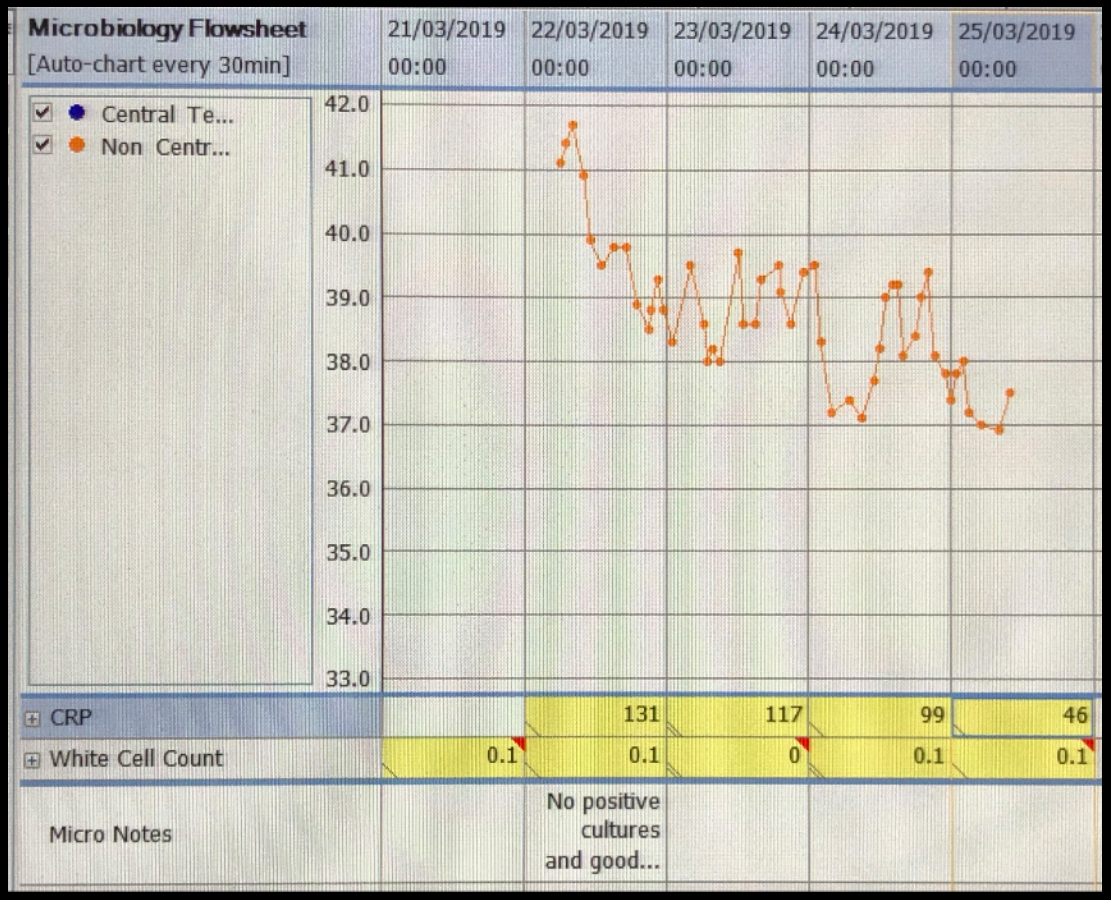
- 25 y.o. female
- AML -> bone marrow transplant -> 6/12 oral GVHD -> worsened -> ICU

5 days' post-admission

15 days' post-admission

- ? cause
- no organism isolated, empiric a/b, antifungal, antiviral
- no improvement despite steroids etc..

- 25 y.o. male with lymphoma and high EBV titre post-chemo Rx
- marked pyrexia, high CRP, neutropenia
- not responding to a/b -> ICU



- bilirubin 156, platelets 38 —> ferritin 74,000 —> bone marrow
- diagnosis: haemophagocytic lymphohistiocytosis (MAS)
- Rx: anakinra (IL-1 receptor antagonist)

ICU PATIENTS WITH NEW SIGNS/SYMPTOMS OFTEN TREATED 'ON SPEC' ...
.. AND OFTEN ON TENUOUS GROUNDS

- clinician confidence (or lack of)
- out-of-hours microbiology SpR consult

—> excessive and unnecessary antibiotic use

—> resistance, overgrowth

—> effects on microbiota, mitochondria,

—> toxicity (renal, liver, rash)

CHALLENGES, DIAGNOSTIC CONUNDRUMS, ETC..

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STILL UNCERTAIN ABOUT BEST TREATMENT REGIMEN

ANTIBIOTICS

- cephalosporin with (or without??) macrolide for CAP?
- mono- or combination therapy for HAP or VAP?
  - outcome studies: is death attributable to the HAP/VAP, or not?
  - clinical vs microbiological cure?
- duration of therapy?
  - is 4-5 days sufficient? or shorter?
  - should resistant bugs get longer duration Rx, or not?
  - paranoia around pneumococcal (10-14 days…)

STILL UNCERTAIN ABOUT ADJUNCT THERAPIES

- Corticosteroids
- Immunoglobulins
- Statins
- Other immunomodulatory approaches e.g. GM-CSF, anti-PD1 …
- Modes/types of ventilation - does ECMO saves lives?

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WE NEED BETTER DIAGNOSTICS...

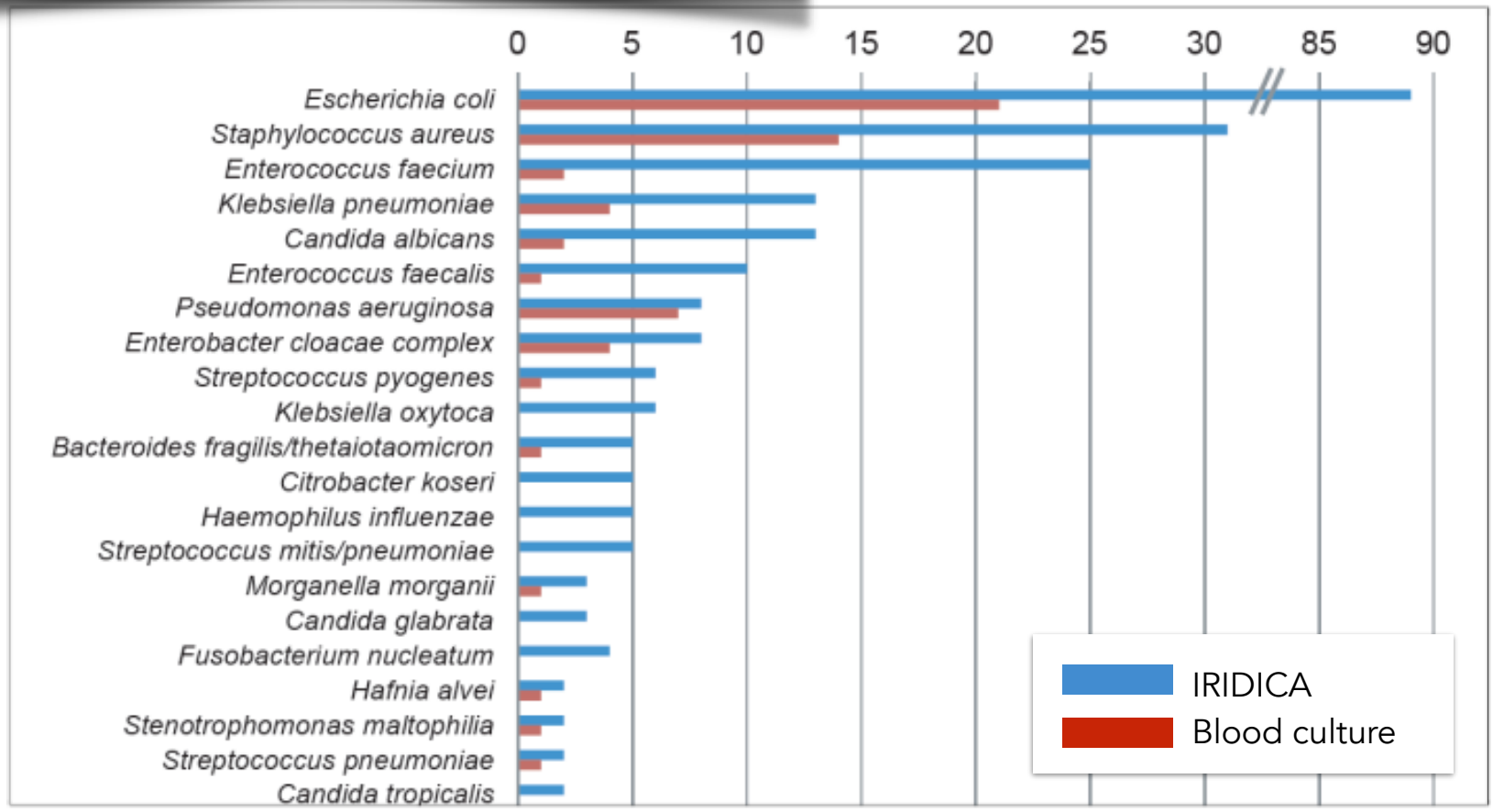
Host

Rapid Diagnosis of Infection in the Critically Ill, a Multicenter Study of Molecular Detection in Bloodstream Infections, Pneumonia, and Sterile Site Infections

Jean-Louis Vincent, MD, PhD, FCCM[1]; David Brealey, MD[2]; Nicolas Libert, MD[3]; Nour Elhouda Abidi, MD[4]; Michael O'Dwyer, MD[5]; Kai Zacharowski, MD[6]; Malgorzata Mikaszewska-Sokolewicz, MD[7]; Jacques Schrenzel, MD[8]; François Simon, MD[9]; Mark Wilks, PhD[5]; Marcus Picard-Maureau, PhD[10]; Donald B. Chalfin, MD, MPH[11]; David J. Ecker, PhD[11]; Rangarajan Sampath, PhD[11]; Mervyn Singer, MD[2]; the Rapid Diagnosis of Infections in the Critically Ill Team

PCR/ESI-MS
6-hour prep time from taking blood culture

(*Crit Care Med* 2015; 43:2283–2291)



PATHOGEN IDENTIFICATION, RESISTANCE, SUSCEPTIBILITY

60-90 mins from blood, urine, sputum ..

T2Biosystems®

3-5 h

T2 Magnetic Resonance

T2Bacteria coverage

Gram Negative:

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii*

Gram positive:

NEGATIVE BACTERIA:

- *inetobacter baumannii*
- *aemophilus influenzae*
- *eisseria meningitidis*
- *eudomonas aeruginosa*
- *terobacteriaceae*
- *terobacter cloacae* complex
- *cherichia coli*

YEAST:

- *Candida albicans*
- *Candida glabrata*
- *Candida krusei*
- *Candida parapsilosis*
- *Candida tropicalis*

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lture

Accelerate PhenoTest™ BC kit

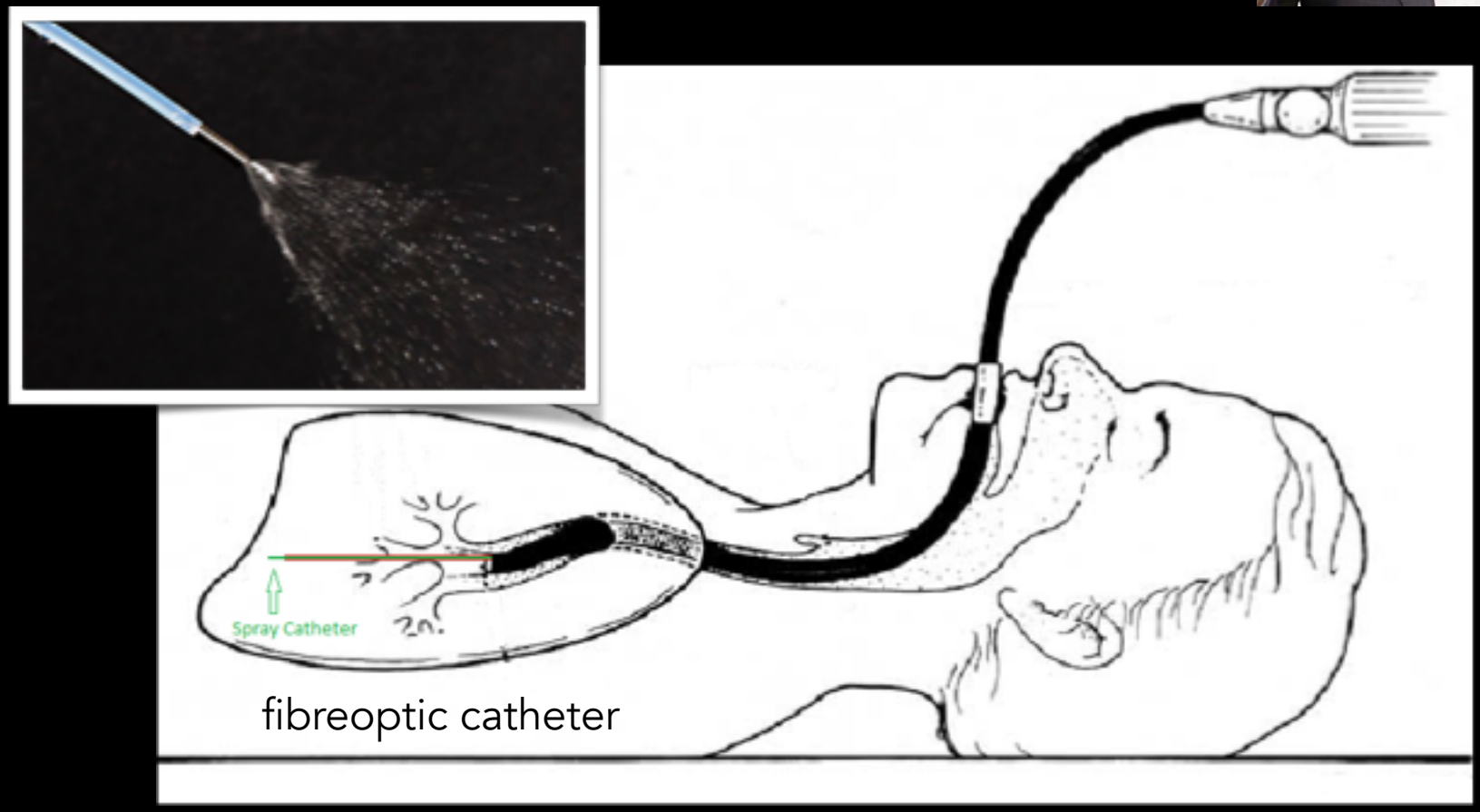
–

Average time to results:
Identification in less than 90 minutes
Antibiotic susceptibility in less than 7 hours

ACCELERATE DIAGNOSTICS™

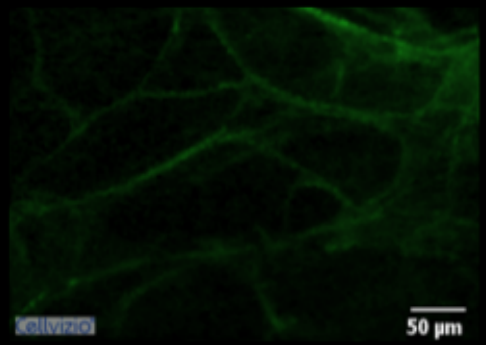
Prof Kev Dhaliwal
(Edinburgh)

OPTICAL ENDOMICROSCOPY

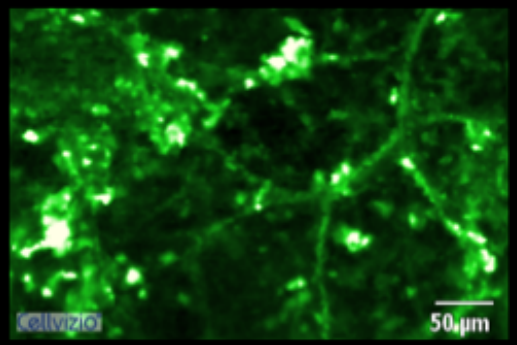


Prof Kev Dhaliwal
(Edinburgh)

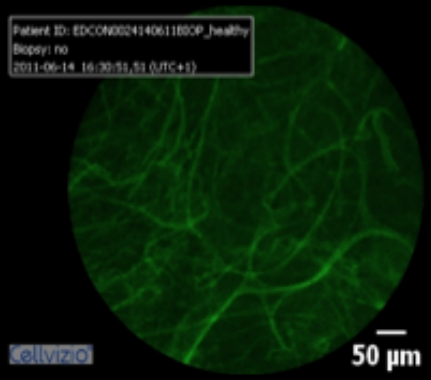
OPTICAL ENDOMICROSCOPY



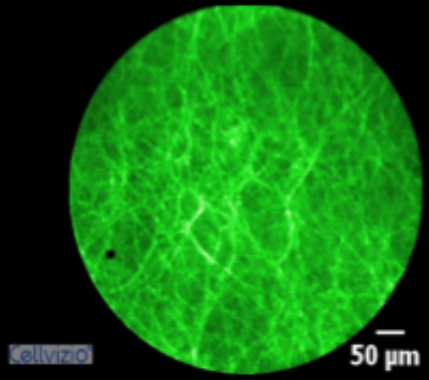
Control



Staph aureus



Heathy control



Fibroproliferation

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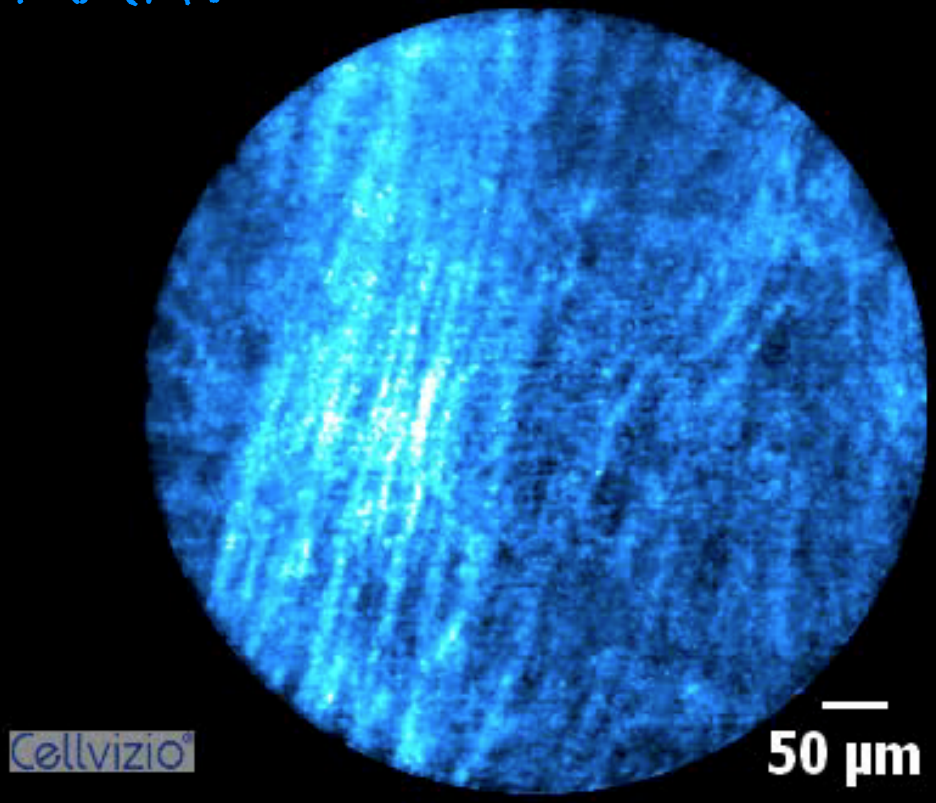
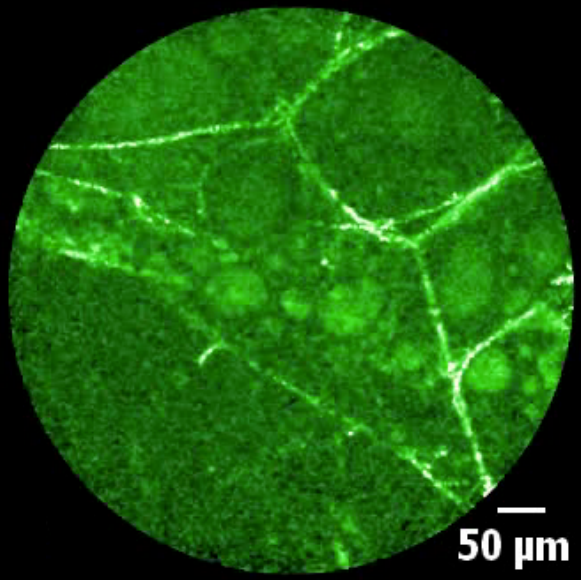
(Edinburgh)

OPTICAL ENDOMICROSCOPY - MAN!

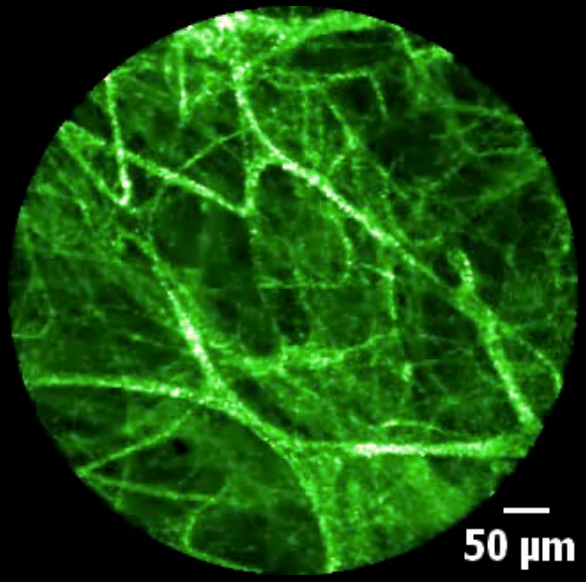


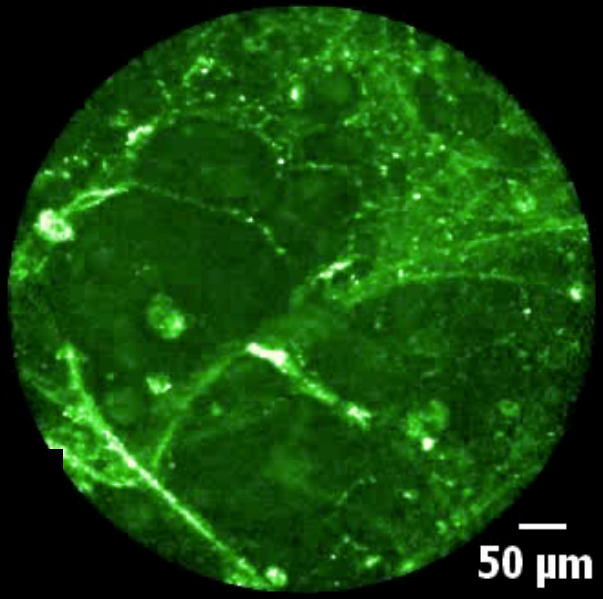
wellcome

OEDEMA



ALVEOLAR COLLAPSE





PNEUMONIA

PCR, MICROFLUIDICS, GOLD NANOPARTICLES, LATERAL FLOW, PHOTONICS, ...

Rapid diagnostics (PCR gene transcripts, ELISA/multiplex (cytokines, proteins..), etc within 60-90 mins

SUMMARY

- different types of infection affect critically ill patients - community vs. hospital (± ventilator)-acquired, healthy vs. immunosuppressed …
- still struggle to rapidly identify underlying pathogen
- .. and whether infection is actually present or not (sick patients often highly complex and traditional signs of chest infection often missing)
- still don’t know how best to treat - both antimicrobial and adjunct Rx
- novel diagnostics look very promising to enhance capability