Intensive Care Med (2019) 45:243–245
https://doi.org/10.1007/s00134-018-5272-z

WHAT'S NEW IN INTENSIVE CARE

Infectious diseases: the 10 common truths I never believed

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The field of infectious diseases has caught us with many surprises. Even in the time of modern medicine, evolutionary perspectives on disease biology and management have continued to challenge us from time to time (Fig. 1). Integration of knowledge from various fields of science has opened an exciting arena, ruffling our beliefs learned in medical schools or during practice of clinical medicine. Ten selected topics that developed under the influence of certain evolutionary factors in medicine are presented in Table 1.

Most reports have consistently reported *Streptococcus pneumoniae* as the leading cause of community-acquired pneumonia. However, a recent study performing sensitive molecular assays has analyzed the prevalence of viruses as the cause of severe pneumonia requiring hospitalization and suggesting that rhinovirus is the most prevalent organism [1]. Current management should include the use of multiplex PCR for respiratory viruses in severe episodes, and antiviral therapy (Cidofovir) or enriched immunoglobulins may emerge as new therapies.

For decades, identification and subsequent antimicrobial susceptibility testing have consistently required at least 48–72 h to be informative. Subsequent to the introduction of matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) for routine diagnostic microbiology, identification of bacteria from blood culture is possible as soon as 6 h with a major clinical outcome benefit [2]. Further studies should incorporate rapid diagnostic tests as point of care to identify resistant phenotypes at the bedside.

It is highly suggested to avoid the use of antimicrobials that have tested resistant in vitro. However, for certain infections by carbapenem-resistant *Klebsiella pneumoniae* for which alternative therapeutic options are not available or not proven successful, it is recommended to review the therapy based on minimum inhibitory concentrations (MICs) of carbapenems. For isolates with MICs between 4 and 8 mcg/ml, or even up to 16 mcg/ml, recent reports have suggested that high-dose and extended infusion of carbapenem is a good option when combined with a susceptible agent (such as tigecycline, colistin or fosfomycin) [3]. Recent reports also suggest that the double carbapenems, combining ertapenem-meropenem, could be effective for therapy of infections by carbapenemase-producing *K. pneumoniae* [4].

Traditionally, randomized controlled trials with adjuvant therapy to treat sepsis have not considered the need to personalize prescriptions. Some reports have recently demonstrated that the response to therapy would be very different in some subsets of patients. Further studies should incorporate the newer suggestions

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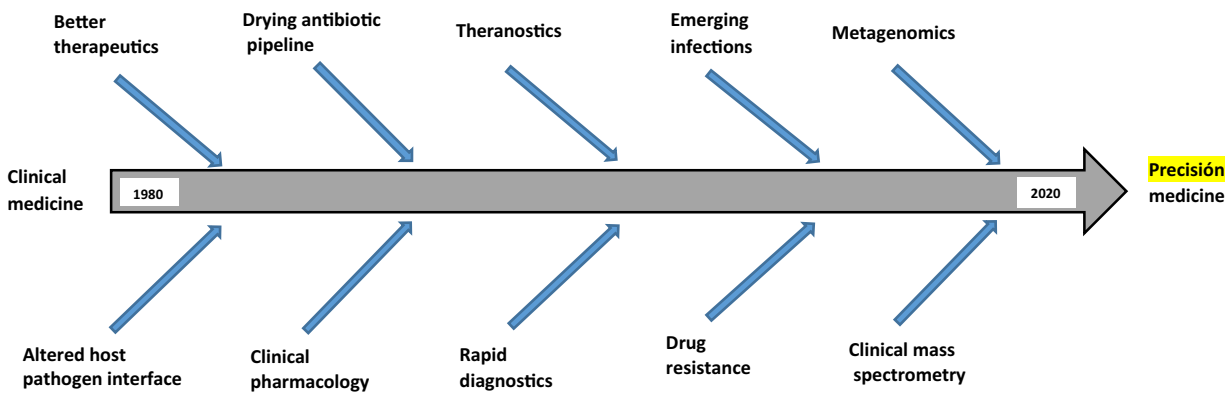

*Factors are not representative of timeline

Fig. 1 Potential factors* contributing to the surprises in infectious diseases presented in the article

Table 1 Ten surprises in infectious diseases

	Topics
1	Respiratory viruses are common causes of community-acquired pneumonia requiring hospitalization
2	MALDI-TOF significantly reduces the time to organism identification in blood
3	Carbapenenem-resistant *Klebisella pneumoniae* can be treated with carbapenems
4	Identification of drug response phenotypes helps to understand different responses in patients with sepsis
5	Weak evidence to support aerosolization of antimicrobials in respiratory infections
6	Oral cleansing with chlorhexidine may be harmful in intubated patients
7	Colistin is not the solution to treating MDR Gram-negative organisms
8	Therapeutic drug monitoring is required to optimize dosage in bacterial and fungal infections in mechanically ventilated patients
9	Invasive aspergillosis is a life-threating complication after viral pneumonia
10	Pulmonary manifestations are more common complications than bleeding when managing Ebola virus disease (EVD) outside of low- and middle income countries

and perspectives recommended in a position paper from ESCMID toward a personalized management of sepsis [5].

Oral care with chlorhexidine is a cornerstone across many care bundles to prevent ventilator-associated pneumonia. However, recent evidence suggests oral chlorhexidine care may increase the risk of death in general hospital populations. There is also a lack of significant risk reduction for ventilator-associated pneumonia (VAP) among non-cardiac surgery patients, provoking reconsideration of routine use of chlorhexidine [6, 7].

Following the indication of drugs, such as aztreonam or tobramycin in cystic fibrosis subjects, as aerosolization to treat/prevent respiratory infections, many intensivists have used these agents in the form of aerosolization in mechanically ventilated patients to treat ventilator-associated tracheobronchitis or pneumonia. Until recently, it was considered a potential improvement for patients with MDR Pseudomonas or Acinetobacter infections [8]. Observational studies suggested potential efficacy with few reports of adverse events. However, weak evidence was found when focusing on mechanical ventilation. These studies reported a non-negligible risk of bronchospasm, hypoxemia and other respiratory complications. As a consequence, in a position paper the ESCMID considered that the evidence of efficacy was weak and the risk of respiratory adverse events not negligible [9]. Use of mesh-membrane nebulizers and implementation of a standardized research protocol are required. Further studies should use pre-defined clinical outcomes as end points.

A recent study in *Acinetobacter baumannii* VAP reported that adding a loading dose of colistin did not improve pre-defined outcomes but was associated with nephrotoxicity [10]. Other authors agree on the risk of nephrotoxicity due to the low therapeutic margin of polymyxin/colistin when administered for severe MDR infections [11]. Moreover, a recent study on *pneumonia* by

MDR *Pseudomonas* failed to demonstrate improved mortality when colistin (or amikacin) was administered in a cohort of mechanically ventilated patients with pneumonia caused by strains highly resistant to carbapenems (MIC_{50} 16 mg/l) [12]. These patients should receive alternative agents such as ceftolozane-tazobactam, and newer antimicrobials are required. Progression of colistin-susceptible to -resistant strains under antibiotic exposure is increasingly reported in clinical settings, supported by sequencing studies showing high-frequency mutations occurring under selection pressure.

The DALI study was a multicenter observational study conducted in a network of European intensive care units (ICUs), which demonstrated that many patients exposed to label doses of cephalosporins present suboptimal plasma levels falling below PK/PD targets [13]. This is due, in part, to the increase in the volume of distribution associated with mechanical ventilation and septic shock. As a consequence, personalization of dosage in the form of higher dosing, extended infusion or even continuous infusion (for time-dependent drugs) is currently advised.

Pandemic influenza has resulted in better availability of diagnostic techniques for respiratory viruses, which are currently implemented in most ICUs. As a consequence, many episodes of severe pneumonia previously diagnosed as unknown cause have been identified. In parallel, administration of oseltamivir to these patients has become standard of care, whereas it was unlikely prior to the 2009 pandemic influenza. A subset of patients with low CD4/CD18 and thrombocytopenia has been associated with further complications by invasive pulmonary aspergillosis [14]. Preemptive posaconazole administration in those with severe lymphocytopenia has been suggested, and the efficacy should be assessed in further randomized clinical trials.

Management of Ebola virus disease (EVD) has been traditionally limited by the scarce resources of countries where outbreaks occur. The past epidemic outbreak in western Africa has been associated with some patients repatriated to Europe or secondary cases. These subjects were managed in well-equipped ICUs. As a consequence, surviving patients presented better resuscitation strategies; thus, pulmonary edema and acute respiratory distress syndrome have acquired relevance [15].

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Acknowledgements
Authors acknowledge the participation of experts who helped in the choice of the selected topics: Marcio Sa Borges, Rafael Zaragoza, Ricard Jorda and Yolanda Peña-Lopez.

Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflict of interest.

Received: 1 June 2018 Accepted: 5 June 2018
Published online: 22 June 2018

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