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From “infection in intensive care” to “intensive care in infection”: intensive care specialists’ perspective of tropical medicine

Da “infecção em intensivismo” ao “intensivismo em infecção”: o olhar do intensivista na medicina tropical

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Infectious disease medicine and intensive care medicine are two well established areas in the realm of medical knowledge and praxis. The former, much older, has developed and reinvented itself ever since medicine gained consciousness of itself as occupation and art. The second, equipped by contemporaneity, presses forward in large strides creating and consolidating its epistemological statutes, in other words, the manner it deals with the knowledge base that informs its practice. Knowledge gained from the use and generation of scientific evidence, its limits, the line of action when this evidence is absent, the balance intensive care medicine maintains between science and humanization in its practice, its foundations for ethical choices, these things, among others, converge in the intensive care physician’s perspective.

The intersection between these two fields of medicine, both in view of day-to-day medical aspects, as well as in the academic fields of generating knowledge and its transmission through publications and journals, constitutes fertile ground from which at least two conceptually correlated, albeit distinct, fields can arise: the field of ‘infection in intensive care’ and that of ‘intensive care in infection’.

The first has demonstrated great interest in the infections that aggravate the condition of patients under intensive therapy. It would not be wrong to describe this as the infectologist’s perspective of intensive care medicine. It is the field of hospital infections applied to intensive care, with its epidemiological, therapeutic, prophylactic and even administrative issues, (since it affects quality indexes). In this intersection, due attention is given to catheter-induced bloodstream infections, urinary tract infections, surgical-wound infections, pneumonias brought on by mechanical ventilation, the bionomics of microorganisms as well as their evasion and resistance mechanisms, the employment of new antibiotics and antibiotic classes is delineated and the role of fungal agents is increasingly acknowledged in this context.

This editorial, however, is more concerned with the second conceptual field, the field of intensive care in infection. An enormous percentage of infectious diseases is treated within the realm of intensive therapy. Thus, intensive care, along with its epistemology and good practices, plays a fundamental role in the therapy of patients with infectious diseases such as tetanus, malaria, meningococemia and yellow fever. In view of this, infectologists and epidemiologists, who have an extensive history of commitment to these diseases, would do well to adopt the perspective of the intensive care physician.

The importance of intensive care in infectious diseases was perhaps under-emphasized up to, at least, the 1990s when the concepts of sepsis, severe sepsis, septic shock and multiple organ dysfunction syndrome (MODS) were

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established.⁽¹⁾ Once revisited, standardized and clearly defined, these concepts shed light on the fact that the course of all infectious diseases, regardless of their etiology (i.e., viral, bacterial, protozoan or fungal), may evolve adversely to the point of severe sepsis, which, in turn, may evolve to the MODS stage. From another perspective, infectious diseases that behave as severe sepsis/MODS (and any infectious disease can do so) will present a clinical condition comprised of a series of organ and system dysfunctions. As a matter of fact, certain infectious diseases, as a rule, evolve into severe sepsis, at times taking the route of hemorrhagic fevers at times icterohemorrhagic diseases. As a result, the field of tropical medicine coexists with the daily need of clinically combating severe sepsis/MODS.

Regardless of the disease that brought on severe sepsis, whether it be yellow fever, leptospirosis or hantavirosis, it will evolve (or not) into a reduction of the sensorium, reduced urinary output, impaired tissue perfusion, hyperlactatemia, acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), thrombocytopenia, hemorrhagic diathesis and disseminated intravascular coagulation (DIC); hypotension with hyperdynamic states and low systemic vascular resistance index (SVRi) and high cardiac index (CI); and high direct bilirubin due to trans-infection cholestasis.

Whatever the origin of severe sepsis, be it meningococemia or malaria, it will still require early target-guided restoration of perfusion achieved by administering the same crystalloid fluid and vasoactive amines that are to be found in any intensive care unit. Early antimicrobial therapy stands as an unquestionable principle in these cases in which the same ventilation protective strategy, the same blood glucose control, and the same physiological-dose corticosteroid may (or may not) be employed. In such cases, if drotrecogin alpha is available, its use is to be determined whenever applicable and sensible.

'To employ or not' is the great issue that stands to be examined through the perspective of the intensive care physician who generates knowledge and guidelines. In what measure, and along with which precautions and peculiarities can the general recommendations for severe sepsis/MODS be applied to severe sepsis in tropical disease patients? The knowledge, abilities, attitudes and practices of good intensive care medicine, that converge in an intensive care physician's perspective, have a direct impact on the praxis of caring for patients with severe infectious diseases. May this perspective also impact the generation of knowledge and its communication through publications and journals, which is not only appropriate and desirable, but even essential. In view of this, this edition of RBTI, containing the review article

by Gomes et al., 'Severe *Plasmodium falciparum* malaria,'⁽²⁾ is an extremely timely, if not pioneering effort, not only for covering a tropical disease that has a high epidemiologic impact in Brazil and around the world, but also, and foremost, for considering it as the severe sepsis it is. From their intensive care physician's perspective, the authors present this theme appropriately for intensive care specialists, infectious-intensive medicine specialists, and general physicians, who need to be equipped to deal with this disease, which is one of the greatest killers of the Brazilian and worldwide population of tropical region inhabitants, both in pre-intensive as well as intensive therapy contexts.

Thus those who specialize in tropical medicine should be increasingly concerned with acquiring the perspective of intensive care physicians (and vice-versa) in order to develop their praxis. Following this rationale, let us consider some specific instances as examples, and certainly not under the pretension of exhausting the subject of tropical diseases, which is of such great importance worldwide and in Brazil.

Yellow fever is an endemic disease in Brazil. There is a classic form of the disease that is clinically characterized by fulminant hepatitis or, in the vocabulary of intensive care specialists, acute liver failure, which is highly lethal and reaches 70% mortality rates. What weapons does the intensive care specialist have at his disposal when professionally called upon to treat a patient with classic yellow fever? To what extent are early management bundles⁽³⁾ and overall acute liver failure recommendations effective in these patients? What treatments are proposed for the upper digestive hemorrhages ("black vomits") and hepatorenal syndromes that affect these patients?

Some will superficially discard this disease as being rare. However it must be remembered that Brazil is at ESPIN (public health emergency) status for yellow fever, since this disease is unquestionably making its way in large paces towards Brazilian southern and eastern states. Previously concentrated in the forest regions of the legal Amazon (including Maranhao State) and mid-western states, the disease is currently found in the forest regions of southern Piaui State, western Bahia State and the entire State of Minas Gerais, western Sao Paulo State, and the states of southern Brazil. Extensive border regions in neighboring Argentina and Paraguay face the same yellow fever epidemic issue.

The most recent autochthonous outbreaks in Sao Paulo State, advanced the forest transmission zone to the borders of the *Serra do Mar* coastal mountain range. If the endemic zone continues progressing as it has, Brazil may find itself up against outbreaks in the densely populated regions such as its shore-side municipalities which, for historic reasons, have had greater population densities. Yellow fever has not

yet returned to urban localities, that is, transmission has not been reported in urban, non-forested areas, but this presents a real possibility and concern over its potential is not unreasonable. Measures have been taken to preclude this from happening through well succeeded concrete epidemiological surveillance efforts, the monitoring of sentinel events (e.g. the deaths of monkeys) and the judicious use of immunobiological products, such as the yellow fever vaccine.

Dengue another tropical flavivirus infection emerged in Brazil at the close of the last century. It has progressively spread through the country, as well as internationally, and concern over dengue tends to increase. This has led to the elaboration, by the Brazilian Association of Critical Care Medicine, of guidelines that have recently and pioneeringly appeared in the RBTI.⁽⁴⁾

This disease is caused by one of four discrete viral serotypes (DEN 1, 2, 3 and 4); three of which three classically move in cyclic patterns throughout Brazil. At times, a single serotype circulates in a given region, while, in others, more than one serotype may co-circulate. This co-circulation increases the probability of patients contracting more than one type of dengue over their lifetime. And when contracted for the second or third time, dengue presents a greater risk as the result of immunologic enhancement mechanisms. Thus, the incidence of severe forms of the disease is increased by co-circulation, and this describes the current Brazilian scenario. It is worth noting that DEN 4 has recently begun circulating in the Amazon region and in Sao Paulo state, which has led to specific surveillance and reporting efforts.

Dengue has variable clinical presentations. Classical dengue has a low mortality risk. It is usually self-limited and

spans from oligosymptomatic forms up to exanthema and maculopapular and petechial forms with mild hemorrhagic features. There are, however, severe forms that may evolve to severe sepsis and shock (mistakenly labeled 'hemorrhagic dengue' and 'dengue shock syndrome'). These labels (and, thus, the clinical presentations) need to be revised from the perspective of the intensive care specialist. The evolution of severe dengue involves increased capillary permeability, leading up to hemoconcentration which serves as a severity marker. How can medicine label a disease as "hemorrhagic" when it has an increased hematocrit as its severity marker? And, with regard to this hemoconcentration, with what measures and to what degree should perfusion be restored? Would Rivers' targets be applicable for these patients?

In addition, some severe cases of dengue include major visceral involvement, behaving as classical yellow fever cases, and resulting in severe and frequently midzonal liver damage. Should this (unnamed) subgroup be treated with different measures than those applied to the so-called hemorrhagic subgroup?

There are, thus, many unanswered questions (whose answers will not be intuitive) which can be summarized in the following question: up to what extent can the generated knowledge and the rationales for actions and recommendations that are employed in severe sepsis/MODS be applied in the management of severe tropical sepsis that evolve into hemorrhagic and icterohemorrhagic forms? Addressing this issue with regards to the production and communication of knowledge is a timely task, one that requires that intensive medicine employ its epistemological and methodological perspective in its analysis of tropical medicine. This is an invitation.

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