Setting The Scene

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Introduction

Intensive care medicine of today is almost unrecognizable when compared to its humble beginnings following the polio epidemics of the 1950s. This relatively young field of medicine is growing at such a pace that it is interesting, and indeed important, to speculate on how we will be practicing intensive care medicine 10 years from now.

In this chapter, I will focus on what has altered in the last 50 years in various aspects of intensive care medicine. Playing Devil’s advocate somewhat, I will consider changes in each field from a positive and negative viewpoint. Looking into the recent past (and the present) raises many questions and many uncertainties, but sets the stage for the future, and I believe that we must use the past to define future priorities.

Intensive Care in General

The Optimist’s View

The quality of intensive care has improved over time; changes have not necessarily been made in great strides, but multiple small improvements have led to a progressive reduction in morbidity and mortality. Despite the altered population of intensive care patients with more elderly, more debilitated, and more immunosuppressed patients being treated, there is some evidence that mortality has decreased among patients with sepsis [1] or the acute respiratory distress syndrome (ARDS) [2-4]. The recent rush of guidelines and protocols for everything from administration of sedation to management of septic shock to end-of-life patient management has caused a reduction in the wide variability in medical practice, thus improving its overall quality.

The Pessimist’s View

What actual progress has been made over the last few decades? After all, there has been no outstanding breakthrough, like insulin for diabetes or thrombolysis for acute myocardial infarction, in our field. Indeed, much of the apparent...
progress in intensive care medicine has been borrowed from other specialties, e.g., surgery, immunology, cardiology. We are not even sure that mortality from sepsis and ARDS has decreased substantially [5]. The major development could be said to be a decrease in iatrogenic events as we have realized the negative impacts of some common interventions (Table 1). However, with newer therapies, invasive monitoring, and more complex interventions, we have also increased the potential for iatrogenicity.

**Mechanical Ventilation**

The Optimist’s View

Early respirators were large, unwieldy pieces of equipment that delivered established minute ventilation at a given, fixed rate. Modern machines are increasingly streamlined and portable and provide the physician with an almost unlimited range of ventilatory modes and options that enable mechanical ventilation to be targeted at individual patients and adjusted according to their needs and response. Improved understanding of the use and potential of non-invasive mechanical ventilation has enabled the rates of endotracheal intubation, and consequently the risks of ventilator-associated pneumonia (VAP), to be reduced [6]. This technique can even decrease mortality rates in patients with hypercapnic respiratory failure [7, 8].

The Pessimist’s View

Modern respirators have so many options and knobs that they can be difficult to use and it takes some time to become familiar with each new machine. Indeed, many of the options are never used at all! The development of newer ventilatory modes, such as pressure support ventilation, has not been shown to improve outcomes. The success of non-invasive mechanical ventilation just demonstrates the risk of iatrogenic complications due to our interventions. However, we still do not know how best to apply non-invasive mechanical ventilation or which patients will benefit most from it. While it does seem to be beneficial in hypercapnic respiratory failure, what about in non-hypercapnic respiratory failure? More questions remain unanswered than have been answered.

**Acute Respiratory Failure**

The Optimist’s View

Major advances have been made in our understanding of respiratory mechanics, and application of this knowledge has improved outcomes. For example, large tidal volumes, long considered as useful to improve tolerance and prevent the development of atelectasis, have been shown to promote inflammation and worsen outcomes in ARDS [9]. Patients both with and without ARDS are now being managed with lower tidal volumes than in the past [10].
The Pessimist’s View

The optimal respiratory conditions for the patient with ARDS remain undefined. What is the optimal tidal volume, level of positive end-expiratory pressure (PEEP), or alveolar recruitment strategy? Respiratory monitoring systems at the bedside are unimpressive, and pharmacological interventions including surfactant [11], inhaled nitric oxide [12], and anti-inflammatory agents [13] have not been shown to reduce mortality. Even prone positioning, although shown to improve gas exchange, has not been shown to definitely improve outcome [14].

Sepsis Therapies

The Optimist’s View

Better understanding of the complex network of mediators involved in the immune response to infection has led to the development of new strategies specifically targeted against sepsis. The development of new drugs in sepsis has certainly not been a smooth ride. Still, one new agent, activated protein C, has been licensed for use in patients with severe sepsis and septic shock and has been shown to decrease mortality [15]. Now, other new agents will certainly follow. Many others are already in the pipeline and several are currently undergoing clinical trials. Combinations of these agents in the future will further improve outcomes.

The Pessimist’s View

The list of negative studies of sepsis therapies is actually far more impressive than the list of positive studies. Particularly notable have been the negative results from clinical trials of agents that had been clearly shown to improve outcomes in pre-clinical and sometimes even in phase I and II clinical trials, for example, endotoxin antibodies [16, 17], anti-tumor necrosis factor (TNF) strategies [18], and interleukin-1 receptor antagonist [19]. For all the time and money that has been expended in this field, only one agent has been licensed, activated protein C, and even with this drug, the survival advantage remains limited, and high costs restrict its use.

Steroids in Septic Shock

The Optimist’s View

The use of massive doses of methylprednisolone to limit the inflammatory response, which failed to improve outcomes [20], has been replaced by the concept of relative adrenal insufficiency, leading to the administration of low doses of hydrocortisone in septic shock, which has been shown to reduce mortality rates [21].
The Pessimist’s View

The evidence for relative adrenal insufficiency is actually not so strong. The study by Annane et al. [21] was not entirely positive (significant differences were obtained only after adjustment for several factors), so that the potential benefits of corticosteroid administration in septic shock is not yet convincingly proven [22]. Moreover, the need for an ACTH test is unsettled. In the study by Annane et al. [21], many patients had received etomidate to facilitate endotracheal intubation, and this product is known to alter adrenal function. Hence, there is a need for further study to finally answer some of these questions (the Corticus prospective, double-blind, multicenter study of hydrocortisone in patients with septic shock is ongoing).

Vasopressin Administration In Septic Shock

The Optimist’s View

Vasopressin is one of the most important endogenous stress hormones during shock, and increased interest in metabolic alterations during sepsis has led to the realization that vasopressin levels are inappropriately low in patients with severe sepsis and this phenomenon may contribute to the hemodynamic perturbations that are characteristic of septic shock [23]. Addition of vasopressin to standard vasopressors, such as norepinephrine, can improve hemodynamic status [24] and recent guidelines for the management of patients with septic shock support its use, at low infusion rates of 0.01-0.04 units/min, in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressors [25].

The Pessimist’s View

There is no demonstrated outcome benefit associated with administration of vasopressin in patients with septic shock. Some studies have suggested that while vasopressor agents may increase arterial pressure, some agents are also associated with worsened outcomes [26]. ICU physicians have been too quick to jump on the vasopressin bandwagon, starting to administer vasopressin widely before real evidence of benefit was established. Trials are currently underway to define the potential benefit of administration of low doses of vasopressin in septic shock, but in the meantime, are we again creating an iatrogenic effect?
Oxygen Delivery

The Optimist’s View

Dobutamine has taken first place in our list of inotropic agents; we have learned to use it not only in low flow states, but also whenever oxygen delivery may be insufficient. So-called ‘pre-optimization’, raising oxygen delivery to supranormal values, may be beneficial in high-risk surgical patients, especially when it involves the correction of underlying hypovolemia [27].

The Pessimist’s View

The maintenance of supranormal oxygen delivery has not been shown to improve outcomes in critically ill patient populations as a whole, and excessive administration of fluids and inotropic agents may be harmful [28]. Studies on pre-optimization have been usually performed in the United Kingdom but whether the results apply to other settings is largely unexplored.

Early Goal-Directed Therapy

The Optimist’s View

The importance of aggressive early and complete resuscitation has been established in severe sepsis/septic shock [29] as in severe trauma. Rivers et al. [29] randomized 263 patients with severe sepsis or septic shock to receive, for the first six hours after admission, either standard resuscitation or early goal-directed therapy in which fluids, vasoactive agents, and red blood cells were given to optimize central venous pressure, arterial pressure and hematocrit and then dobutamine to achieve a target central venous oxygen saturation (ScvO2) of at least 70%. This strategy resulted in markedly lower mortality (30.5% compared to 46.5% in the standard care group, p = 0.009), and similar protocols are now implemented in many institutions and are included in recent recommendations regarding optimal management of the patient with severe sepsis [25].

The Pessimist’s View

The study by Rivers et al. [29] was a single-center study, performed not in an ICU, but in an emergency department. Before applying such a protocol to all patients, we need to know more about it. Importantly, the reasons for the improvement in outcome seen in this study are not clear; maybe the treatment was simply suboptimal in the control group; perhaps the improved outcomes were related to the choice of target, i.e., ScvO2; possibly they were due to the increased use of fluids and/or dobutamine and/or blood transfusions in the treatment group.
Again, many questions remain and we should not be too keen to jump in until we have at least some of the answers.

Hemodynamic Monitoring

The Optimist’s View

Criticism of the pulmonary artery catheter has been met by the development of a number of less invasive monitoring devices, including esophageal Doppler, transesophageal echocardiography, arterial waveform analysis, and thoracic impedance. Using functional hemodynamic monitoring to define responsiveness in the optimization of blood flow improves outcome in cardiac surgery patients [30].

The Pessimist’s View

The use of invasive hemodynamic monitoring has certainly been challenged repeatedly in recent years [31-33] and its use has decreased over the last decade. However, although the use of pulmonary artery catheters has not been shown to improve outcome from critical illness, they have not been shown to worsen outcomes either. The development of less invasive monitoring techniques is to be applauded, but can they be shown to improve outcomes? Indeed, has any monitoring device been shown to improve outcomes? Every ICU patient is attached to multiple machines with assorted alarms, but where is the evidence that they decrease mortality? Even if we accept that such monitoring is useful, the assessment of fluid responsiveness by pressure tracing or stroke volume variation has a number of limitations, and is potentially useful only in mechanically ventilated patients, who are well sedated, without arrhythmias, and ventilated with relatively high tidal volumes [34].

Glucose Control

The Optimist’s View

Sometimes relatively small and simple strategies can provide big benefits. For example, blood sugar control, maintaining blood glucose at or below 110 mg per decilitre, has been shown to decrease mortality in a mixed group of ICU patients, primarily surgical, many being admitted after cardiac surgery [35]. Although the practicalities of such an approach make it difficult to apply routinely, it is now widely recommended that blood glucose levels should be kept below 150 mg/dl [25].
The Pessimist’s View

The beneficial effects of tight glucose control have been shown in only one single-center study, with many postoperative patients after cardiac surgery. Moreover, the associated caloric intake in these patients was quite high. The results still need to be confirmed in large multicenter trials with broader patient populations (large scale studies are ongoing).

Nutritional Support

The Optimist’s View

Nutrition has only relatively recently begun to take a key place in ICU patient management, but patients are now fed much sooner and better than in the past with the realization of the importance of good nutrition on outcomes. Indeed, diet can influence both disease development and recovery. Enteral feeding is widely accepted as being superior to parenteral feeding [36, 37] and much has been learnt about dietary requirements including the realization that excessive feeding can be as harmful as inadequate nutrition [38].

The Pessimist’s View

Despite improved awareness of feeding issues in the critically ill, we still do not know when to start and how best to feed the patient. Trials of modified solutions, including the so-called immuno-enhancing diets, have not demonstrated improved survival over standard feeding solutions [39-41]. The fact that enteral feeding is preferable to parenteral should not surprise us, being further evidence of a negative iatrogenic event. Even when using the enteral route, overzealous feeding may promote gut ischemia [42, 43], and can result in complications including aspiration with potential increased risks of nosocomial pneumonia. Indeed, we are now being encouraged to consider the concept of ‘underfeeding’.

Selective Decontamination of the Digestive Tract

The Optimist’s View

The gut may be an important source of microorganisms, which can be involved in the development of nosocomial infection, in particular, VAP. After many years of debate and discussion, selective decontamination of the digestive tract (SDD) was shown to decrease hospital mortality (24% vs 31%, p=0.02) in a randomized controlled trial in Holland [44].
The Pessimist’s View

SDD certainly decreased mortality rates in this study [44], but it was conducted in a single ICU in a country with low rates of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant enterococci (VRE). Therefore, the results may not immediately apply to other institutions with greater antimicrobial resistance rates [45]. In addition, despite this study and others supporting the use of SDD, it is not widely applied, mainly because of fears of encouraging bacterial resistance, the development of which may not be apparent for months or even years after its introduction.

Hygiene Measures

The Optimist’s View

The use of routine hygiene measures, such as hand washing before and after patient contact [46, 47], antibiotic rotation [48], shorter course antibiotic treatments [49] and using barrier precautions when inserting intravascular catheters [50], have all been shown to reduce the incidence of nosocomial infections, and the introduction of infection control protocols can result in sustained reductions in nosocomial infections [51].

The Pessimist’s View

The problem of nosocomial infections is getting worse, largely due to the excessive use of antibiotics (especially broad spectrum ones) and the lack of adequate infection control procedures. In particular, it is well recognized that washing hands is a very effective way to prevent the spread of bacteria, but still compliance among personnel is poor [52–54]! Increasingly nosocomial infections are associated with multiresistant organisms with higher morbidity and mortality, which has even led to the temporary closure of some units [55].

Sedation

The Optimist’s View

We have swung from an attitude which supported widespread use of large doses of sedative agents to keep patients comfortable, and even to make patient care easier, to a much more conservative approach with the realization that excess sedation can be harmful. Studies have shown that daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation reduces ICU length of stay and decreases the incidence of complications of critical illness associated with prolonged intubation and mechanical ventilation [56].
The Pessimist’s View

The widespread use of sedatives and the realization that more can be too much provides yet more evidence of iatrogenic complications!

Management of Liver Failure

The Optimist’s View

The increased use of liver transplantation and improved transplantation techniques and post-operative management has changed outcomes from acute liver disease [57, 58]. The development of extracorporeal systems, such as the molecular adsorbent recirculating system (MARS) system, may further decrease mortality rates [59].

The Pessimist’s View

Progress in the field has been related to the development of liver transplantation, including use of living donors, but medically there has been no progress at all. The use of extracorporeal systems is expensive, and although there are promising results from small studies [59], they have not been shown to improve outcomes [60].

Cardiopulmonary Resuscitation

The Optimist’s View

Wider availability of defibrillators has changed the outcome from out-of-hospital cardiac arrest (most commonly due to ventricular fibrillation) [61]. Amiodarone has replaced lidocaine in the management of life-threatening ventricular arrhythmias after lidocaine use was associated with increased mortality. Vasopressin has taken its place as a potent and reliable vasoconstrictor in profound hypotension during cardiopulmonary resuscitation (CPR) and is recommended as an alternative to epinephrine in current guidelines [62].

The Pessimist’s View

Little progress in cardiopulmonary resuscitation has been achieved, especially in the ICU. Even the superiority of vasopressin over epinephrine has not been shown conclusively [63]. Any progress that has been made is due to simplified guidelines and increased involvement of bystanders in starting effective CPR.
Polytrauma

The Optimist’s View

Studies have shown that resuscitation should not necessarily be too aggressive [64], as massive fluid administration may increase bleeding, by increasing intravascular pressures, disrupting clot formation and diluting coagulation factors. The use of factor VIIa may decrease bleeding rates in trauma [65].

The Pessimist’s View

The suggestion that too much fluid early in trauma resuscitation can be detrimental [64], again demonstrates our tendency to encourage iatrogenic complications of therapy with overzealous reactions. Furthermore, restricting fluid administration may limit oxygen delivery and contribute to the development of multiple organ failure (MOF). In addition, such an approach is deleterious in the presence of cerebral lesions, where arterial hypotension can have disastrous consequences on brain function. Studies on factor VIIa have shown that this strategy may limit the need for blood transfusions, but no effect on outcome has been demonstrated.

Severe Head Trauma and Cerebral Resuscitation

The Optimist’s View

Considerable advances have been made in cerebral monitoring with the development of local brain tissue oxygen monitoring and microdialysis techniques to assess brain metabolic data [66, 67] and mortality rates from severe head trauma have fallen [68, 69]. Induced mild hypothermia may be an option to protect the neurons in hypoxic encephalopathy and has been associated with improved outcomes [70–72].

The Pessimist’s View

Despite advances in monitoring, none has actually been shown to improve outcomes and as good markers of cerebral damage are still lacking, the evaluation of cerebral lesions remains largely based on the Glasgow coma score. Evaluation of cerebral blood flow and oxygen availability at the bedside is still difficult, and in terms of new therapies, nothing has been proven. The best established intervention is hyperventilation for intracranial hypertension. But, hyperventilation may reduce cerebral perfusion [73] and thereby worsen outcome, again emphasizing the risk of serious iatrogenic complications of some of our interventions. Inducing hypothermia after cardiac arrest is not easy and has not been shown to reduce mortality rates in a randomized multicenter study.
[74], and there is little evidence to support barbiturate therapy either [75]. Steroid therapy, used in head injury patients for years, has recently been shown to worsen outcomes in a multicenter study involving 10,008 patients [76], and craniectomy in severe brain edema may result in increased vegetative states [77].

**Stroke**

**The Optimist’s View**

Thrombolytic therapy, a treatment that improves outcomes in ischemic stroke, has changed the way we treat thromboembolic stroke [78]. Other pharmacological advances have also been made, with administration of factor VIIa being shown to improve outcome from intracerebral hemorrhage [79]. Improved availability of imaging techniques has also helped in diagnosis and management.

**The Pessimist’s View**

The benefit from thrombolytic therapy is limited to early intervention – within 3 hours of stroke onset – and to patients with ischemic stroke. The study of VIIa in intracerebral hemorrhage [79] is only a phase IIb study, and the limited benefit may not warrant the costs of this therapy.

**Renal Failure**

**The Optimist’s View**

The development of continuous hemodialysis techniques has allowed us to avoid the ‘peak and trough’ effect of intermittent dialysis on fluid balance, electrolyte levels, and osmotic shifts. Continuous hemofiltration has evolved into a continuous veno-venous system with relatively complex instruments. We now know that giving diuretics to patients with acute renal failure may increase mortality and worsen renal function [80], especially in the presence of hypovolemia. Low dose dopamine, so-called renal dose dopamine, does not prevent renal insufficiency in critically ill patients [81] and should be abandoned as a routine practice.

**The Pessimist’s View**

So, more evidence that our interventions cause iatrogenic problems; diuretics and low dose dopamine are both harmful pharmacological interventions. And there is no evidence that hemofiltration techniques improve outcomes in critically ill patients.
**Blood Transfusions**

The Optimist’s View

The use of blood transfusions has declined, especially after an important prospective, randomized Canadian study showing a conservative approach may result in somewhat lower mortality rates [82]. Studies are ongoing to determine the optimal transfusion trigger and techniques to better assess and monitor tissue oxygenation are being developed.

The Pessimist’s View

Yet more iatrogenicity…!

**Other IV Fluids**

The Optimist’s View

Albumin administration has been controversial for decades, as it is hard to demonstrate beneficial effects and the costs are high. Albumin administration has been suggested to result in high mortality rates [83] but a large Australasian study demonstrated that the use of albumin is safe [84]. Studies are evaluating the potentially beneficial effects of artificial crystalloids and hemoglobin solutions on tissue oxygenation.

The Pessimist’s View

The SAFE study showed that for once we have not caused iatrogenic complications! However, although it has been shown to be as safe as saline in the setting of the SAFE study, albumin has not been shown to improve outcomes, and we still do not know if and when to administer it. Hydroxyethyl starch solutions may increase bleeding and alter renal function, gelatin solutions are not very effective and can have allergic reactions, saline solutions may induce hyperchloremic metabolic acidosis, and balanced solutions are hypotonic! And where do hypertonic solutions fit in? There is still a lot to be done to evaluate the best type of i.v. solution.

**Process of Care**

The Optimist’s View

Critical care medicine is better organized now than at its start and many countries now recognize intensive care medicine as a specialty in its own right.
Established treatment protocols for standardization of care have resulted in markedly improved outcomes, reduced costs, and minimized medical errors.

The Pessimist’s view

Protocols are developed primarily to avoid iatrogenic problems and to restrict the liberty of the practitioner to make decisions based on their experience.

**Medical Emergency Teams**

The Optimist’s View

The development of medical emergency teams (METs), also known as hospital outreach or rapid response teams, has extended the principles of critical care medicine to a hospital-wide approach, and has been associated with reduced complications after major surgery, reduced ICU admissions, and improved outcomes [85, 86].

The Pessimist’s View

METs provide a neat cover up for the lack of emergency medicine training of doctors and nursing staff in the hospital; staff should be better trained rather than replaced.

**Conclusions**

From an optimist’s viewpoint, one could say that the last 50 years has seen great progress in intensive care medicine, perhaps not by any single, tremendous development(s), but by a succession of small steps, which together combine to give us an intensive care service to be proud of, providing quality care for many thousands of patients each year. However, the pessimist would perhaps say that much of the apparent progress in intensive care medicine has come about through the identification and correction of our own iatrogenic effects. It is indeed rather worrisome to realize that that many of our interventions may have had some deleterious effects. This notion has been suggested for mechanical ventilation (especially with high tidal volumes), blood transfusions, and excessive sedation (Table 1). We have increasingly realized that non-invasive is better than invasive and less is better than more. Patients are better treated without endotracheal intubation, with minimal sedation, without excessive use of vasopressor or inotropic agents.

These two viewpoints are both valid, although the true picture perhaps lies somewhere between the two. As with Janus, intensive care medicine has two faces, one looking backwards and the other towards the future. This is not a bad
thing and indeed progress has, and can, come from learning from the past and applying those lessons to the future.

Clearly many questions remain unsettled and pose a challenge for the years to come. There is, however, one key point that we have not discussed and that is the role of the intensive care doctor. Here we can only be optimistic: the ICU doctor has made a difference! Closed ICUs under the responsibility of an ICU physician have lower morbidity and mortality rates than open units [87–89]. Proper training of the intensive care doctor must therefore remain a key priority for the future, and with the projected future shortage of ICU physicians [90] we need in addition to develop alternative strategies, such as telemedicine.

References


Table 1. Some potentially harmful iatrogenic interventions

- Excessive antibiotic use
- Iatrogenic fluid overload
- Excessive administration of inotropic agents
- Ventilation with too high tidal volumes
- Excessive sedation
- Use of invasive hemodynamic monitoring
- Unnecessary use of antiarrhythmic agents
- Excessive caloric intake
- Too liberal blood transfusions
- Traumatic effects of endotracheal intubation and airway management