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Year in review in Intensive Care Medicine 2011: III. ARDS and ECMO, weaning, mechanical ventilation, noninvasive ventilation, pediatrics and miscellanea

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Acute respiratory distress syndrome and extracorporeal membrane oxygenation

Several articles have addressed important aspects of the acute respiratory distress syndrome (ARDS) and its treatment.

The incidence and outcome of ARDS in the era of lung protective ventilation have been evaluated by Villar and colleagues [1] in a 1-year prospective, multicenter, observational study, under the acronym ALIEN (Acute Lung Injury: Epidemiology and Natural History). The study was conducted in 13 geographical Spanish areas, which serve a population of 3.55 million of adults. A total of 255 mechanically ventilated patients fulfilled the ARDS definition, representing an incidence of 7.2/100,000 population/year. Pneumonia and sepsis were the most common causes of ARDS. At the time of meeting ARDS criteria, mean PaO_2/FiO_2 was 114 ± 40 mmHg, mean tidal volume was 7.2 ± 1.1 ml/kg predicted body weight, mean plateau pressure was 26 ± 5 cmH_2O, and mean positive end-expiratory pressure (PEEP) was 9.3 ± 2.4 cmH_2O. Overall ARDS intensive care unit (ICU) and hospital mortality was 42.7% (95% CI 37.7–47.8) and 47.8% (95% CI 42.8–53.0), respectively, suggesting that despite the use of lung protective ventilation, overall ICU and hospital mortality of ARDS patients is still higher than 40%.

A couple of articles dealt with lung recruitment in patients with ARDS. Dellamonica et al. [2] compared two methods to evaluate PEEP-induced lung recruitment, one based on the pressure–volume curve (considered as gold standard) and the other based on the bedside end-expiratory lung volume (EELV) measurement using the nitrogen washout/washin technique. PEEP-related strain was also assessed at two levels of PEEP, low and high. Recruitment assessed with the two techniques was well correlated. In addition, the ratio between PEEP-induced lung volume changes (ΔEELV) and functional residual capacity differentiated high from low recruiters (110 vs. 55%). Strain increased with PEEP and was larger in high recruiters.

Arnal et al. [3] assessed the dynamics of lung recruitment and the hemodynamic changes during a recruitment maneuver (sustained inflation at an airway pressure of 40 cmH2O maintained for 30 s) in 50 patients with ARDS. Most of the recruitment occurred during the first 10 s of the recruitment maneuver (mean time constant for lung volume increase was 2.3 ± 1.3 s), while arterial pressure decreased significantly after 10 s. The authors concluded that a duration of 10 s may be recommended for a sustained inflation to achieve sufficient lung recruitment while preventing hemodynamic compromise. This article was discussed in an editorial by Marini [4]. The protective ventilatory strategy may fail in the treatment of ARDS. Under this condition other therapeutic strategies can be attempted.

Charron and colleagues [5] reported the characteristics and prognosis of patients with severe lung injury (PaO_2/FiO_2 <100 mmHg after 24–48 h of mechanical ventilation) who are routinely ventilated in the prone position using a low stretch ventilation strategy. In this monocenter study, the authors provide data of 218 patients with ARDS admitted between 1997 and 2009. Of these patients, 57 (26%) were positioned prone because of a PaO_2/FiO_2 <100 mmHg after 24–48 h of mechanical ventilation. Prone sessions lasted 18 h/day, and 3.4 ± 1.1 sessions were required to obtain an FiO_2 <60%. The 60-day mortality was 19%, and death occurred after 12 ± 5 days. Logistic regression analysis showed that among the 218 patients, PP appeared to be protective with an odds ratio of 0.35 [0.16–0.79]. It was concluded that routine prone positioning is feasible in patients with a PaO_2/FiO_2 <100 mmHg after 24–48 h, and suggest that this strategy is protective and has a high survival rate.

In patients with ARDS, the combined use of high frequency oscillation (HFO) and tracheal gas insufflation (TGI) improves oxygenation versus standard HFO. Mentzelopoulos and colleagues [6] hypothesized that HFO + TGI would reduce the amount of nonaerated lung tissue in the dependent lung. Authors studied 15 patients who had ARDS, and they were submitted to a whole-lung CT scan after lung-protective conventional mechanical ventilation (CMV) and after 45 min of HFO and 45 min of HFO + TGI. They found that HFO + TGI versus HFO and CMV resulted in a lower percentage of nonaerated lung tissue (mean ± SD, 51.4 ± 5.1% vs. 60.0 ± 2.5%, and 62.1 ± 9.0%, respectively; $p \leq 0.04$); this was due to HFO–TGI-induced recruitment of nonaerated tissue in the dependent and nondependent lower lung. In addition, HFO + TGI significantly improved oxygenation versus HFO + TGI. It was concluded that HFO + TGI improvement in oxygenation occurs through a mechanism of recruitment of previously nonaerated lower lung units.

The most severe cases of ARDS not responding to conventional and advanced treatments need to be approached through extracorporeal membrane oxygenation (ECMO).

In a interesting study Nair and colleagues [7] describe the technical challenges, efficacy, complications, and maternal and infant outcomes associated with ECMO for severe ARDS in pregnant or postpartum patients during the 2009 H1N1 pandemic. This retrospective observational study, conducted on seven tertiary hospitals in Australia and New Zealand, studied 12 patients (7 pregnant and 5 postpartum). Their median [interquartile range (IQR)] age was 29 (26–33) years; 6 (50%) were obese. Two patients were initially treated with veno-arterial (VA) ECMO. All others received veno-venous (VV) ECMO with one or two drainage cannulae. ECMO circuit-related complications were rare, circuit change was

needed in only two cases, and there was no sudden circuit failure. Bleeding however was common, leading to large volumes of packed red blood cell transfusions [median (IQR) volume transfused was 3,499 (1,451–4,874) ml] and was the main cause of death (three cases). Eight (66%) patients survived to discharge. The survival rate of infants whose mothers received ECMO was 71%, and surviving infants were discharged home with no sequelae. It was concluded that ECMO is effective, with outcomes comparable to those of non-pregnant patients and acceptable infant outcomes.

Another interesting study [8] described the development and results of a retrieval program developed in New South Wales (NSW), Australia, to provide ECMO for the safe transport of adults with severe, acute respiratory or cardiac failure, from 1 March 2007 to 1 June 2010. Forty adult patients were retrieved on ECMO support (median age 34 years). The indications for retrieval were respiratory in 38 patients (of whom 16 were confirmed or suspected H1N1 cases) and cardiac in two patients. Two other patients died after referral but before ECMO support could be established.

Patients were transported by road (65%), medical retrieval jet (25%) and helicopter (10%). Thirty-four patients (85%) survived to hospital discharge. There were no deaths or major morbidity associated with these retrievals. It was concluded that severe respiratory failure, which was considered to preclude conventional ventilation for safe transfer to tertiary centers, was managed by an ECMO referral and retrieval program in NSW and had a high rate of survival. This program also enhanced the capacity of the state to respond to a surge in demand for ECMO support due to the H1N1 epidemic.

A multicenter Italian study [9] reported the organization and results of a national ECMO network (ECMOnet) that was set up in view of the expected 2009 influenza A (H1N1) pandemic. The network consisted of 14 ICUs with ECMO capability and was set up to centralize all severe ARDS patients to the ECMOnet centers assuring safe transfer. Between August 2009 and March 2010, 153 critically ill ARDS patients (53% referred from other hospitals) were admitted to the ECMOnet ICU with suspected H1N1. Sixty patients received ECMO according to ECMOnet criteria (and 28 were transferred while on ECMO). Survival to hospital discharge in patients receiving ECMO was 68%. The length of mechanical ventilation prior to ECMO was an independent predictor of mortality. It was concluded that a network organization based on preemptive patient centralization allowed a high survival rate and provided effective and safe referral of patients.

Weaning

Patient-ventilator interaction during pressure support ventilation (PSV) and proportional assist ventilation plus [PAV+] were compared in a physiological study involving 11 patients difficult to wean [10].

During three consecutive trials [a first trial of PSV (PSV1), followed by PAV+, followed by a second PSV trial (PSV2), with the same settings as PSV1], patients' mechanical and respiratory patterns were evaluated. Compared to PAV+, during PSV trials, the mechanical inspiratory time [Ti(flow)] was significantly longer than patient inspiratory time [Ti(pat)] ($p < 0.05$); Ti(pat) showed a prolongation between PSV1 and PAV+, and PAV+ significantly reduced expiratory trigger delays [delay(trexp)] ($p < 0.001$).

The portion of tidal volume (VT) delivered in phase with Ti(pat) [VT(pat)/VT(mecc)] was significantly higher during PAV+ ($p < 0.01$). The time of synchrony was significantly longer during PAV+ than during PSV ($p < 0.001$). During PSV, 5 patients out of 11 showed an asynchrony index (AI) greater than 10%, whereas the AI was nil during PAV+. The authors concluded that PAV+ improves patient–ventilator interaction, significantly reducing the incidence of end-expiratory asynchrony and increasing the time of synchrony.

Rozé et al. [11] evaluated a method for setting neurally adjusted ventilatory assist (NAVA) during weaning, with the NAVA level adjusted to obtain 60% of the maximal diaphragmatic electrical activity (EAdi) measured during a spontaneous breathing trial (SBT). This method proved to be feasible and well tolerated, allowing for a progressive reduction of NAVA level during weaning.

A second study [12] compared the effect of NAVA and PSV on patient–ventilator interaction in 22 intubated patients (COPD 36%). Patient–machine synchrony was better with NAVA, as demonstrated by the lower number of asynchronies per minute and the reduction in the number of patients with asynchrony index >10%. Improvement concerned particularly the inspiratory trigger delay, ineffective efforts, and premature and late cycling off. Finally, Tuchscherer et al. [13] assessed the feasibility of a prolonged application of NAVA in patients with critical illness-associated polyneuromyopathy. As compared with healthy subjects, these patients showed a prolonged phrenic nerve latency and a decreased diaphragm compound muscle action potential. Nevertheless, NAVA could be applied in 13/15 patients for up to 3 days, with stable breathing pattern, hemodynamics and gas exchange while preserving respiratory drive.

Two articles dealt with the prediction of weaning outcome in mechanically ventilated patients. Zapata et al. [14] evaluated the ability of B-type natriuretic peptides (BNP) to predict and diagnose weaning failure from cardiac origin. Thirty-two out of 100 patients failed a SBT, 12 because of heart failure and 20 because of respiratory failure. BNP and NT-proBNP were higher before SBT and increased significantly during SBT in patients failing because of heart failure. BNP performed

better than NT-proBNP for prediction and diagnosis of weaning failure from cardiac origin.

Sellares et al. [15] compared clinical characteristics and outcomes of patients with simple, difficult and prolonged weaning, and assessed predictors for prolonged weaning and survival in 181 mechanically ventilated patients. Patients with simple (43%) and difficult (39%) weaning had similar characteristics and outcomes, while those with prolonged weaning (18%) had a higher incidence of COPD, more complications and worst outcomes. Heart rate $\geq$105/min and $PaCO_2$ $\geq$54 mmHg during SBT predicted a prolonged weaning. In addition, reintubation and hypercapnia during SBT independently predicted a decreased 90-day survival. These findings were commented on in the editorial by Laghi [16].

When the weaning fails patients may need to be tracheotomized. Fikkers and colleagues [17] in a prospective randomized clinical trial involving 120 patients, compared two techniques of percutaneous tracheostomy: the guide wire dilating forceps (GWDF) and the single step dilatational tracheostomy (SSDT) technique. The early and late outcomes were analyzed. Sixty patients in each group were followed for up to 3 months after decannulation. Most of the reported complications in both groups were minor (58.3% in the GWDF group and 61.7% in the SSDT group). A trend was found towards an higher percentage of major perioperative complications in the GWDF group in comparison to the SSDT group [10.0 vs. 1.7% ($p = 0.06$)], with a comparable long-term outcome.

Mechanical ventilation

Gas conditioning

Zanella et al. [18] compared leakage of fluid across the cuff of different endotracheal tubes in a laboratory bench study. A major finding was that the double-layer guayule latex cuff prevented leakage at tested PEEP levels, from 0 to 15 cmH_2O. The other tubes, cylindrical and conical PVC cuffs as well as polyurethane cuffs did not prevent leakage at zero PEEP, whereas with higher PEEP levels leakage decreased and was absent at the highest PEEP level.

Gas conditioning during mechanical ventilation is an important problem. Moran and colleagues [19] compared the effects of an active heated humidifier (HH) and passive heat and moisture exchangers (HME) on endotracheal tube resistance. Gas conditioning was performed using the HH in 22 patients and the HME in another 22. Patients were matched for endotracheal tube diameter, days of mechanical ventilation, simplified acute physiology score II (SAPS II) and fluid balance. Used-ETT (endo tracheal tube) resistance was measured immediately after extubation. ETT diameters were similar between the HH and HME groups (7.9 ± 0.4 vs. 7.9 ± 0.3 mm; $p = 0.98$), as well as days of mechanical ventilation (11.3 ± 7.7 vs. 9.5 ± 4.5; $p = 0.34$), SAPS II (41.0 ± 13.6 vs. 42.0 ± 11.7; $p = 0.79$) or fluid balance. ETT resistance increased from intubation to extubation: from 6.8 ± 1.1 to 10.6 ± 4.3 $cmH_2O\ L^{-1}\ s^{-1}$ in the HH group ($p < 0.001$) and from 6.8 ± 1.1 to 10.2 ± 3.8 $cmH_2O{\cdot}L^{-1}{\cdot}s^{-1}$ in the HME group ($p < 0.001$). Irrespective of the humidification device there was a 53% average increase in resistive load, suggesting a physiological relevance.

Dead space and CO_2 monitoring

The pathophysiological states of the lung result in an increase in deadspace ventilation and thus in a reduced ventilatory efficiency. A review article examined [20] the current physiological concepts of deadspace and the available methods to assess ventilatory efficiency at the bedside. The Bohr and the Enghoff modifications of Bohr's equation were fully described, as well as the Fowler's method. The authors commented on several indices that either predict deadspace or track ventilatory efficiency at the bedside. They also described the various clinical applications of deadspace measurements in the critically ill patients.

Gancel et al. [21] tested a new transcutaneous CO_2 monitor (TOSCA 500) in patients with acute respiratory failure. Their finding was that the new tool compared well with arterial CO_2 measurements with a mean difference of 0.1 mmHg for a range of values between 23 and 84 mmHg.

Diaphragm activity and gastroesophageal pressures

Barwing and co-workers [22] tested the efficiency of an esophageal EMG catheter for assessing the diaphragm electric activity. This is needed for guiding the ventilator when providing NAVA. They found that PEEP, body position and intra-abdominal pressure may affect the catheter position and the EMG signal. This must be realized when finding the optimal catheter position. However, the authors conclude that they could always get a stable EMG signal.

Demoule et al. [23] analyzed a technique to detect phrenic nerve injuries since such injuries may cause diaphragm dysfunction and impede ventilatory function. They used cervical magnetic stimulation (CMS) to detect a delayed or prolonged phrenic nerve conduction time and compared it with electrical stimulation (ES) as a reference technique. Their findings were that CMS compared well with ES, making CMS an easy and reliable tool at the intensive care unit.

Chiumello and coworkers [24] tested the performance of a new naso-gastric "polyfunctional" double-balloon catheter with one balloon located in the esophagus and the other in the stomach. The catheter performed reasonably well compared with a standard balloon catheter and should facilitate the simultaneous recording of esophageal and intra-gastric pressures. One indication for its use is to enable the distinction between pulmonary and extra-pulmonary ARDS, but there are certainly many more where abdominal pressure is of interest.

Sedation

Spies and colleagues [25] conducted a prospective, two-center, randomized, triple-blind study involving adults requiring mechanical ventilation (MV) for more than 24 h aimed at comparing the quality of analgesia provided by a remifentanil-based regime with that provided by a fentanyl-based regime. Sedation was provided using propofol (and/or midazolam if required). At planned interim analysis ($n = 60$), 50% of remifentanil patients ($n = 28$) and 63% of fentanyl patients ($n = 32$) had maintained target analgesia scores at all time points ($p = 0.44$). There were no significant differences between the groups with respect to mean duration of ventilation (135 vs. 165 h, $p = 0.80$), duration of hospital stay, morbidity or weaning. Interim analysis strongly suggested futility, and the trial was stopped. It was concluded that the use of remifentanil-based analgesia in critically ill ventilated patients was not superior to fentanyl-based analgesia.

Clouzeau et al. [26] assessed the feasibility and safety of sedation with propofol target-controlled infusion during fiberoptic bronchoscopy with bronchoalveolar lavage in 23 hypoxemic patients undergoing NIV. Propofol target-controlled infusion allowed for good tolerance of the procedure without causing any significant adverse effects, including endotracheal intubation (only one patient intubated within 6 h after the procedure). These findings encouraged the authors to perform an ongoing multicentric study with the primary objective of determining if using propofol target-controlled infusion during fiberoptic bronchoscopy under NIV may prevent oxygenation impairment and increase the clinical tolerance of the procedure.

Physiological mechanisms

In an interesting review article Abreu and colleagues [27] presented the recent advances in the field of stem cell biology, highlighting the effects of mesenchymal stem cell therapy in the context of acute respiratory distress syndrome, lung fibrosis and chronic obstructive pulmonary disease. Clinical and experimental studies published in the past 11 years have been analyzed. The authors found data suggesting beneficial effects of mesenchymal stem cells on lung development, repair and remodeling. A number of studies reported that paracrine factors could be effective in reducing inflammation and promoting tissue repair. The mesenchymal stem cell releases several growth factors and anti-inflammatory cytokines that regulate endothelial and epithelial permeability and reduce the severity of inflammation. It was concluded that a better understanding of the mechanisms that control cell division and differentiation, as well as of their paracrine effects, is required to enable the optimal use of bone marrow-derived stem cell therapy to treat human respiratory diseases.

Caironi and colleagues [28] hypothesized that the time course of VILI may be fully explained from a single perspective when considering the insult actually applied, i.e., lung stress and strain. To test this hypothesis, a retrospective analysis of data available in the literature was performed. Studies in which healthy animals were aggressively ventilated until preterminal VILI were selected. Data on morphometry, ventilator settings, respiratory function and duration of ventilation were derived. For each animal group, lung stress (transpulmonary pressure) and strain (end-inspiratory lung inflation/lung resting volume ratio) were estimated. Twenty studies including five mammalian species (sheep, pigs, rabbits, rats and mice) were selected. Time to achieve preterminal VILI varied widely (18–2,784 min), did not correlate with either tidal volume or airway pressure applied, but was weakly associated with lung stress ($r^2 = 0.25$, $p = 0.008$). In contrast, the duration of mechanical ventilation was closely correlated with both lung strain ($r^2 = 0.85$, $p < 0.0001$) and lung strain weighted for the actual time of application during each breath ($r^2 = 0.83$, $p < 0.0001$), according to exponential decay functions. It was concluded that lung strain may play a critical role as a unifying rule describing the development of VILI among mammals with healthy lungs. This article is accompanied by an editorial comment by de Prost et al. [29].

Noninvasive ventilation

Several studies and reviews have been dedicated to the clinical application of noninvasive ventilation (NIV).

Physiological studies

Fodil and colleagues [30] evaluated the role of interface internal volume on the effective deadspace during NIV. To better understand the effects of the geometrical design of interfaces, the authors quantified flow, pressure and gas composition in terms of CO_2 and O_2 at the passage through different types of interface (oronasal mask,

integral mask and helmet). In particular, they postulated that due to specific gas flow passing throughout the interface, the effective dead space added by the interface is not always related to the whole gas volume included in the interface. Numerical simulations, using computational fluid dynamics, were used to describe pressure, flow and gas composition during ventilation with the different interfaces. Between the different interfaces the effective dead spaces differed only modestly (110–370 ml), whereas their internal volumes were markedly different (110–10,000 ml). Effective dead space was limited to half the tidal volume for the most voluminous interfaces, whereas it was close to the interface gas volume for the less voluminous interfaces, suggesting that effective dead space is not related to the internal gas volume included in the interface.

Cammarota and colleagues [31] published a study on a short-term head-to-head physiologic comparison between PSV and NAVA in delivering noninvasive ventilation through a helmet (h-NIV) in patients with postextubation hypoxemic acute respiratory failure. Ten patients underwent three 20-min trials of h-NIV in PSV, NAVA and PSV again. Arterial blood gases (ABGs) were assessed at the end of each trial. Diaphragm electrical activity (EAdi) and airway pressure (P_{aw}) were recorded to derive neural and mechanical respiratory rate and timing, inspiratory ($delay_{TR\text{-}insp}$) and expiratory trigger delays ($delay_{TR\text{-}exp}$), time of synchrony between diaphragm contraction and ventilator assistance ($time_{synch}$), and the asynchrony index (AI). Compared with PSV, with NAVA the mechanical expiratory time was significantly shorter, while the inspiratory time and duty cycle were greater. $Time_{synch}$ was 0.79 ± 0.35 s in NAVA versus 0.60 ± 0.30 s and 0.55 ± 0.29 s during the PSV trials ($p < 0.01$ for both). AI exceeded 10% during both PSV trials, while not in NAVA ($p < 0.001$). The authors concluded that compared with PSV, NAVA improves patient–ventilator interaction and synchrony, with no difference in gas exchange, respiratory rate, and neural drive and timing.

Milan et al. [32] tested different helmets for applying continuous positive airway pressure (CPAP) and found that large helmets with large anti-suffocation valves minimized CO_2 rebreathing during disconnection of the fresh gas supply. The authors also emphasized the need of monitoring and alarm systems to make the use of the helmet as safe as possible.

Continuous positive airway pressure

The role for CPAP in acute cardiogenic pulmonary edema (CPE) from out-of-hospital to cardiac intensive care unit was evaluated by Ducros and colleagues [33] in a randomized multicenter study on 207 patients that were randomly allocated by emergency mobile medical units to receive either standard treatment alone or standard treatment plus CPAP. CPAP was maintained after admission to the ICU. Inclusion criteria were orthopnea, respiratory rate greater than 25 breaths/min, pulse oximetry less than 90% in room air and diffuse crackles. The primary endpoint was assessed during the first 48 h and combined death, presence of intubation criteria, persistence of either all inclusion criteria or circulatory failure at the 2nd hour or their reappearance before 48 h. Absence of all criteria defined successful treatment. CPAP was used for 60 min in the pre-hospital setting and 120 min in the ICU, and was well tolerated in all patients. Treatment was successful in 79% of patients in the CPAP group and 63% in the control group ($p = 0.01$), especially for persistence of inclusion criteria after 2 h and for intubation criteria. CPAP was beneficial irrespective of the initial $PaCO_2$ or left ventricular ejection fraction, suggesting that immediate use of CPAP in out-of-hospital treatment of CPE and until CPE resolves after admission significantly improves early outcome compared with medical treatment alone.

Noninvasive pressure support ventilation (NIPSV) and CPAP are indeed both used as supportive treatment for CPE. Nouira and colleagues [34] hypothesized that NIPSV would be better than CPAP in terms of clinical benefit. They conducted a prospective, randomized, controlled study in 200 patients (CPAP 101 patients and NIPSV 99 patients). The primary outcome was combined events of hospital death and tracheal intubation. They found a hospital mortality of 5.0% for NIPSV and 2.9% for CPAP ($p = 0.56$). The need for intubation was 6% patients in the NIPSV group and 3.9% in the CPAP group ($p = 0.46$). It was concluded that CPAP does not affect primary clinical outcome in patients with CPE. This article is accompanied by an editorial comment [35].

Cammarota et al. [36] compared different regimes of non-invasive ventilatory support by a Venturi mask or by CPAP in patients with hypoxemic respiratory failure due to either unilateral or bilateral lung involvement. The authors found that CPAP with a pressure of 10 cmH_2O was better in oxygenating blood than breathing with a Venturi mask and also normalized $PaCO_2$ in patients with bilateral affection. Adding a sigh (25 cmH_2O for 8 s) improved further oxygenation in bilateral but not in unilateral lung involvement. Thus, recruitment maneuvers may be useful also during CPAP if there is a bilateral lung affection.

Specific settings of application

Postoperative pulmonary complications occur in 5–10% of all surgical patients. Chiumello and colleagues [37] carried out a systematic review to determine the efficacy of NIV versus standard therapy to treat or prevent postoperative pulmonary complications. Twenty-nine randomized controlled trials were analyzed. Noninvasive ventilation

improved arterial blood gases in 15 of the 22 prophylactic and in 4 of the 7 therapeutic studies; it also reduced the intubation rate in 11 of the 29 studies, and improved outcome in only 1. It was concluded that early administration of noninvasive ventilation could be considered as a prophylactic and therapeutic tool to improve gas exchange in postoperative patients.

Noninvasive ventilation NIV is increasingly used as a palliative strategy when endotracheal ventilation is deemed inappropriate. In this context, palliative NIV can either be administered to offer a chance for survival or to alleviate the symptoms of respiratory distress in dying patients. However, the implementation of palliate noninvasive ventilation remains a controversial issue. In the August issue a review on this subject was published [38] that analyzed ten studies published between 1992 and 2006, including 458 patients who received palliative NIV. The authors found that the technique was feasible, usually well tolerated and half of the patients survived. The potential benefits and harm from noninvasive ventilation in patients who are not eligible for endotracheal ventilation are also discussed. It was concluded that the use of palliative noninvasive ventilation is recognized, but qualitative data (patient comfort, end-of-life process, family burden and health-care provider satisfaction) are still insufficiently reported.

Noninvasive ventilation is an interesting option to avoid reintubation in patients at risk for extubation failure. In this kind of patient, Dimassi et al. [39] compared the short-term physiologic effects of NIV and intrapulmonary percussive ventilation (IPV), a high-frequency ventilation modality that can be superimposed on spontaneous breathing and has the potential to decrease respiratory muscle loading. As compared to spontaneous breathing, indexes of diaphragmatic effort (transdiaphragmatic pressure and the pressure-time product of the diaphragm) and respiratory rate decreased with both NIV and IPV. IPV was, however, less effective than NIV in improving alveolar ventilation.

Oxygen therapy

Two articles dealt with oxygen administration in critically ill patients. In the first, De Graaff et al. [40] retrospectively evaluated 126,778 arterial blood gas data from 5,498 mechanically ventilated patients and assessed clinicians' response to hyperoxia (PaO_2 >120 mmHg). Hyperoxia occurred frequently (22% of arterial blood gases), but FiO_2 was decreased in only 25% of cases. In particular, ventilator settings were not modified when FiO_2 was ≤0.4. This article was accompanied by an editorial by Branson [41]. In the second paper, Sztrymf et al. [42] evaluated the efficacy and safety of nasal high flow oxygen therapy in 38 adult, spontaneously breathing patients with hypoxemic acute respiratory failure. Nasal high flow oxygen was well tolerated and improved oxygenation while decreasing respiratory rate, heart rate and dyspnea. In nine patients nasal high flow oxygen failed and endotracheal intubation was required; these patients had a higher respiratory rate, lower oxygenation and persistence of thoraco-abdominal asynchrony. According to the authors, these results provide sufficient data to launch a randomized controlled study to investigate whether nasal high flow oxygen therapy reduces intubation in patients with hypoxemic acute respiratory failure.

Pediatrics

PICU organization and outcomes

Randomized clinical trials in pediatric critical care are frequently difficult to establish and complete, for reasons that include the relatively small number of children who become critically ill. High-value data that have the potential to change practice are, however, increasingly available through the interrogation of large pediatric critical care databases and registries such as the Dutch Pediatric Intensive Care Evaluation registry and the UK PICANET registry (www.picanet.org.uk). Visser and colleagues [43] identified all infants admitted to Dutch pediatric intensive care units over a 4-year period with confirmed diagnoses of intracranial bleeding due to vitamin K deficiency (VKDB), demonstrating superior case detection than that achieved with the existing standard surveillance system. The study demonstrated clearly the potential usefulness of the PICE registry, and by inference other large national registries, in monitoring the ongoing incidence of specific conditions, including relatively rare conditions such as VKDB. Such ongoing surveillance-associated analysis has the potential to provide evidence of changing outcomes as new clinical treatments or care pathways are introduced especially in areas where conventional clinical trials may prove difficult or unweildy. While the application of information technology (IT) in health care is often assumed to be innovative and therefore to 'improve' care, this is not always the case. It is, however, increasingly evident that careful design and implementation of IT-based systems can confer substantial benefits in some areas of patient care. In pediatric critical care, drug prescription is complex due to the need for multiple dose calculations based on weight or surface area electronic prescribing systems (EPS) with high-level decision support, have the potential to reduce prescribing and errors, and are effective in ensuring planned drug doses are administered as recently demonstrated by Warrick et al. [44]. While single-center studies of IT-based critical care innovations are of limited value, as with large 'national' databases, larger scale studies incorporating standardized data sets and definitions have

the potential to generate powerful data aimed at proving clinical or financial benefit, therefore providing a solid foundation for the diffusion of the IT into the wider health-care community. Collaborative approaches to IT-led improvement in pediatric critical care can only be strongly encouraged.

Brown et al. [45] evaluated the match or mismatch between workload in a pediatric intensive care unit and the medical staffing levels available over 24-h periods. Key events included in the evaluation were admissions, severity of illness on admission, cardiac arrests and ECMO cannulations. One of their key findings was that there was an increase in the adjusted risk of death for admissions occurring between 2000 and 0159 h, at a time when lower concentrations of staff were available and patients admitted had higher Pediatric Index of Mortality 2 scores. While much of the information gained from this study is mainly of local interest there is a clear message: a simple evaluation such as this can be used to identify deficiencies in staffing structures in an objective manner and used to inform construction of staffing models aimed at better matching patient flows and acutity, thereby improving patient safety and outcomes.

The vast majority of children admitted to PICUs are neonates or infants, so standard follow-up 'patient satisfaction' surveys used in adult care cannot be used. Parents' experiences of pediatric intensive care are important not only in assessing 'satisfaction' with their opinions about the care of their children, but also their more deeply lived experiences as parents living through the often traumatic and emotional experince of their children's critical illness. Two papers from Latour and colleagues [46, 47] have recently added to our knowledge in this important aspect of care. Firstly Latour and colleagues sought to investigate the in-depth experiences of parents during the admission of their child to one of seven participating Dutch PICUs. Thirty-nine mothers, 25 fathers and 41 children were interviewed 1 month after their child's discharge from the PICU. Thematic analysis was used to sort quotations from these interviews into sub-themes and further into main themes: attitude of professionals, coordination of care, emotional intensity, information management, environmental factors and parent's participation in care. This study identified key areas of importance, which Latour and colleagues then used to develop and psychometrically test a questionnaire (the EPATHIC questionnaire) to measure parent satisfaction. The construction and testing involved input from 2,046 parents from 8 Dutch pediatric intensive care units, addressing questions within 5 domains: information, care and cure, organization, parental participation and staff attitude. The final questionnaire emerged with 65 statements after rigorous content, validity and performance against embedded 'gold standard' questions. Although well validated in a Dutch population, this questionnaire will require further testing and possible modification if it is to be used in different populations. These studies highlight the huge emotional complexity of pediatric critical illness for parents as well as children, and the rigor needed to develop meaningful tools to assess 'satisfaction' in such a complex care pathway.

Cardiopulmonary resuscitation

Unlike adults, asphxia is a common cause of cardiac arrest in children, although few data are available on its evolution and resolution. Lopez-Herce used an infant animal model of asphyxial cardiac arrest to follow the evolution of cardiopulmonary arrest in 71 anesthetized infant piglets following cessation of ventilation [48]. During asphyxia severe arterial and tissue hypoxia, hypercapnia and lactic acidosis developed rapidly. Bradycardia, hypotension, and increasing PVR and SVR were observed. During CPR arterial, cerebral and tissue oxygenation and hemodynamic parameters were rapidly corrected with return of spontaneous circulation. A further study from the same group [49] compared outcomes from asphyxial cardiac arrest in a similar infant piglet model. Piglets were randomized to receive either continuous chest compressions and non-coordinated ventilation or chest compressions alone. Nine minutes of basic resuscitation was completed in both groups of piglets followed by standard advanced resuscitation measures for up to a total of 30 min. Although neither of the basic CPR protocols achieved adequate oxygenation and ventilation, piglets in the ventilation group had better blood gas and cerebral oxygenation parameters than those in the CPR-only group. Resuscitation in infants and children is importantly different in many respects from adult resuscitation. Although firm recommendations for improved resuscitation techniques for children cannot be drawn directly from these two studies alone, they contribute importantly to the scientific literature on pediatric resuscitation literature and will certainly inform further studies and analyses. The use of ECMO during pediatric resuscitation has been increasingly reported [50] and enthusiastically adopted in many centers. Nevertheless, it has become increasingly apparent that the duration of CPR prior to the commencement of ECMO is an important factor in determining patient outcomes, with lower survival [51] and higher risk of poorer neurological outcomes (Sivarajan VB et al. ICM 2011) being associated with longer pre-ECMO resuscitation times.

Cardiovascular topics

There is increasing interest in the use of sildenafil in the treatment of neonatal and pediatric diseases with associated pulmonary hypertension [52, 53]. Until recently, the lack of a suitable intravenous preparation of the drug has

restricted the ability of intensivists to evaluate its use in the sickest children. Fraisse et al. [54] have recently published a preliminary report of the use of IV sildenafil in children with pulmonary hypertension following surgical repair of congenital heart disease. Although the study was heavily underpowered, the use of IV sidenafil was associated with reduced pulmonary artery pressures and shortened time to extubation. These findings alone are insufficient to support recommendations of routine use of IV sildenafil in clinical practice, but should encourage further exploration of the drug in pediatric and neonatal applications.

Hebbar and colleagues [55, 56] published two important papers in 2011 related to the use of corticosteroid management in shock. In their first paper, the authors investigated the incidence of absolute and relative adrenal insufficiency in a retrospective study of 78 children with SIRS and vasopressor-dependent shock. They determined that absolute and relative adrenal insufficiency was prevalent in this cohort of children and that its incidence increased with age. Introduction of steroids was associated with a significant reduction in vasopressor duration and dosage, and the authors hypothesized that low-dose adrenocorticotropin testing may help further delineate populations of children with shock who require steroid supplementation. In this journal, the authors added to these findings by reviewing a retrospective cohort of 97 children with SIRS and shock to determine the effect of adding fludrocortisone (FLU) to hydrocortisone (HC) treatment. Fifty-two percent of the children included met defintions for sepsis. Septic children who received HC + FLU required vasopressor support for significantly shorter durations than those who received HC alone ($p = 0.011$). As in adults, the debate on if or when, in whom and with what to supplement endogenous steroids in children with shock states continues to rage. High-quality randomized clinical trials are needed here.

Two studies published in the journal during 2011 explore innovative monitoring applications in pediatric critical care. In a small study, Kuhlwein et al. [57] prospectively studied ventilation-induced arterial and central venous pressure variations in a group of 20 critically ill children. This preliminary study identified that increasing peak inspiratory pressure significantly increased ventilation-induced variations in systolic pressure, pulse pressure and central venous pressure. As ventilation-induced variations in arterial pressure have been shown to predict volume responsiveness in critically ill adults, similar studies of this concept in children are eagerly awaited. Teng et al. [58] assessed an adult-approved continuous flow monitoring device, the Flo Trac/Vigileo (Edwards Life Sciences), in children, comparing the device against pulmonary artery catheter-derived thermodilution cardiac output measureents. One hundred thirty-six comparisons were studied in 36 children ranging in age between months and 16 years in whom the two devices were deployed; all had diagnoses of either cardiomyopathy or pulmonary hypertension. There was poor agreement between PAC and Flo Trac measurements, and therefore the utility of the Flo Trac in children remains uncertain. As the benefits of goal-directed therapeutic impact of flow measurements in children are themselves disputed, further developments in this field are keenly awaited.

Nosocomial infection

Central venous catheters (CVCs) are widely used in critical care; 238,000 are estimated to be inserted each year in the UK [59]. CVCs are associated with an increased risk of nosocomial blood stream infection (BSI), which is acknowledged to be an important cause of mortality, morbidity, increased length of stay and substantial extra costs for pediatric patients [60, 61]. Ahead of a multicenter randomized-controlled trial, Harron et al. undertook a survey of all UK pediatric intensive care units to determine which of eight interventions commonly adopted to lower the incidence of CR–BSI were in use and explored whether lack of child-specific evidence explained variances. They uncovered widespread variations in practice, which were at least in part explained by the lack of evidence from pediatric studies on important issues including the safety and efficacy of chlorhexidine skin preparations in young children. They recommended that national or international guidelines on the prevention of CR-BSI should specifically address issues relevant to pediatric practice, supporting these with reports of the quality of evidence and the strength of the recommendations based upon them. Rey et al. [62] reported on factors influencing the occurrence of CR-CBSI from a large propsectively studied cohort of critically ill children. They reduced their CR–BSI rate from 11.94 per 1,000 catheter days to 3.05 per 1,000 catheter days when measures to limit insertion times and measures to reduce the use of parenteral nutrition were introduced to supplement standard insertion and care guidelines. Roeleveld [63] reported on the prevalence of ventilator-associated pneumonia (VAP) in children following cardiac surgery. The incidence of VAP detected was 1.7 per 1,000 ventilator days, a higher figure than has been reported in general PICU populations [64]. The only independent factor associated with the onset of VAP was a higher severity of illness score (PRISM III >10). It remains to be shown from other studies whether children following cardiac surgery are at greater risk of developing VAP or whether this result simply reflects local or other unexplored factors.

Immunoparalysis, defined by prolonged monocyte human leukocyte antigen DR depression, is associated with adverse outcomes in adult sepsis. Hall et al. [65] performed a multicenter cohort trial of children with multi-organ dysfunction syndrome (MODS). In phase 1 of

their study, they determined that immunoparalysis occurred in 34% of the 70 MODS children. In a second study period nonneutropenic, nontransplant patients with dysfunction of >3 organs and with ex vivo LPS-induced TNFa response <160 pg/ml on day 3 of MODS were eligible for enrollment in a prospective, randomized, open-label GM-CSF study, a factor that has been shown to revere immunoparalysis in adult sepsis. All seven of the children receiving standard care developed nosocomial infection with 2/7 deaths. In contrast, the seven children randomized to GM–CSF therapy showed reversed immunoparalysis in <7 days and experienced no nosocomial infections ($p < 0.05$) or deaths. No GMCSF-related adverse events were observed. This small open-label study appears to offer the prospect of a powerful intervention for critically ill children with severe sepsis, but its potential usefulness needs to be addressed in carefully configured randomized controlled trials.

Sedation and analgesia

Delirium is probably underdiagnosed and is a poorly understood problem in pediatric intensive care. Janssen and colleagues [66] explored the validity of using the pediatric anesthesia emergence dilrium (PAED) scale, DRSR-98 and DRS-88 scales in a PICU setting. They found that only the PAED instrument performed well in the assessment of delirium in critically ill children against a clinical gold standard, a structured neuropyschiatric assessment. Now that a suitable assessment tool is available for the assessment of delirium in critically ill children, further studies of its management and prevention are urgently needed. Dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, exhibits potent sedative, anxiolytic and mild analgesic effects without respiratory depression [67]. Its use in adult critical care has recorded several apparent benefits including opioid and benzodiazepine-sparing effects, and a reduced incidence of delirium and withdrawal syndromes. Its use in children is less well established, although early reports suggest that it may confer similar benefits to those seen in adults [68]. The report published recently in the journal from Le and colleagues [69] disappointingly failed to demonstrate any benefit from the addition of dexmedetomidine to standard peri-operative sedative–analgesic agents in children undergoing cardiac surgery. Although relatively large numbers of children were studied, the retrospective sequential cohort design of this study is a major weakness, as is its failure to formally assess the incidence of delirium and the occurrence of haemodynamic side effects such as hypotension and bradycardia. Despite this negative report, dexedetomidine is, as others have shown, of great interest to pediatric intensivists, but requires further study.

Respiratory disease and respiratory support

Respiratory failure and respiratory support are recognized as the key element of all critical care, be it for newborns, infants, children, teenagers or adults. The journal is fortunate to continue to attract excellent papers from neonatology. Two recently published studies illustrate both the value and the challenges of studies in the sick neonate. Tsapis undertook a study to determine the threshold value between normal and reduced dynamic compliance (Cdyn) in ventilated near-term newborns using the algorithm built into their neonatal ventilator (Draeger 8000plus). A population of 30 newborns without pulmoanry disease and 30 with respiratory distress syndrome was studied. Receiver-operating characteristic curves for height-adjusted Cdyn were contructed. A cutoff value of 2.02 ml/mbar.m was determined (sensitivity 100%, specificity 96%) to differentiate between normal and decreased lung compliance. The validation of ventilator-derived values under field conditions supports the use of similarly derived compliance data in the clinical management of the ventilated newborn [70]. Cogo and colleagues [71] report on the need for re-dosing with surfactant in preterm newborns, linking surfactant kinetics to clinical and respiratory parameters. Although not reported in this study, it is logical to speculate that the measurement of dynamic compliance described by Tsapis would be a worthwhile parameter to follow in preterm neonates potentially requiring surfactant re-dosing.

Recent years have seen the expansion of respiratory support options for patients of all ages. Several papers published in the journal in 2011 related to the application of use of noninvasive respiratory support in children in situations where traditional management would have been invasive ventilation. Williams and colleagues [72] described the use of bi-level positive airway pressure (BiPAP) started in the emergency department in children <20 kg with acute exacerbations of asthma. Their report covered 165 children with moderate or severe asthma. No patients died, and none exhibited worsening hypoxia or pneumothorax. Sixty percent were admitted to the PICU where BiPAP continued for a mean of 6.6 h (range 0–47 h). The authors conclude that the use of BiPAP in the emergency management of acute asthma warrants further prospective investigation. James and colleagues [73] reviewed the case records of 83 children who commenced NIV in an attept to avoid intubation, of whom only 36% required intubation. Failure of NIV was independently associated with higher respiratory rates before commencement of NIV. Patients with respiratory diagnoses were more likely to be successfully supported with NIV than patients with oncologic disease, especially those with sepsis. The report of Piastra [74], showing that the number of failing organs predicts failure of NIV, is consistent with the report of James and adds further depth to

knowledge in this expanding area of interest [75]. Although NIV technologies in many indications are relatively recent, its usefulness in bronchiolitis has been accepted, although relatively poorly supported by high quality studies. The reports of Essouri and Schibler provide good contemporary evidence for the use of nasal continuous positive airway pressure (nCPAP), Essouri [76] showing that a level of nCPAP of 7 cmH_2O provides optimal off-loading of respiratory muscles, with Schibler [77] demonstrating that a high-flow nasal cannula system was successful in avoiding ventilation in 4% of a group of infants with bronchiolitis.

The mechanisms of neonatal and childhood critical lung diseases are difficult to study for logistical and sometimes ethical reasons. Meconium aspiration syndrome (MAS) is a life-threatening peri-natal inflammatory lung condition. Pancreatic secretory phospholipase A2 (sPLA2-lB) and proinflammatory cytokines are believed to be central in the genesis of MAS. De Luca and colleagues [78] undertook a study of specific phospholipases and their modulators in broncho-alveolar lavage fluid and meconium from 5 control neonates and 5 babies with meconium aspiration syndrome, and showed that locally produced pulmonary phospholipase (sPLA2) contributes to total phospholipase activity during MAS. Lubrano [79] reported on the prognostic value of the extravascular lung water index (EVLWI) in critically ill children with acute respiratory failure, and its relationship to indices of oxygenation and ventilation. Children with lower EVLWI on admission and a fall in EVLWI in the first 24 h of admission were associated with survival. As a survival indicator, EVLWI measured by the PiCCO device (Pulsion Medical Systems) displayed good sensitivity and specificity, and correlated well with indices of oxygenation, fluid overload and pulmonary permeability. Whether in fact routine measurement of EVLW is useful in guiding the assessment and fluid replacement therapy in children with ARF has yet to be determined.

Borik [80] reported an elegant study to test the hypothesis that RNA editing is altered in children with cyanotic congenital heart disease, and to determine whether adenosine-to-inosine RNA is correlated to a child's postoperative clinical course. The authors have previously shown the occurrence of changes in A-to-I RNA editing in a cell line subjected to hypoxic conditions [81]. The key findings of their recent report in the journal are that cyanotic heart disease is associated with higher rates of A-to-I RNA editing than acyanotic children. Adjustments that follow hypoxia take place on several planes, including increased ventilation and cardiac output, a switch to anaerobic metabolism, improved vascularization and enhanced oxygen-carrying capacity by hemoglobin. Thus, it is possible that the epigenetic process of A-to-I RNA editing is also involved on various levels of cellular adaptation to cyanosis.

Renal and metabolic

The great debate surrounding the management of glycemia in the critically ill continues unabated. A report from Hill eloquently describes the pitfalls of blood glucose measurement in pediatric critical care and their implications for clinical trials of glucose control. Importantly, the authors stress that inaccurate measurements may mask hypoglycemia, and therefore obscure or prevent any potential benefit from control of glycemia emerging from a clinical trial [82].

Finally, the difficulty of defining and quantifying fluid overload in pediatric critical illness is addressed by Selewski [83]. In a simple study the authors showed that both weight-based and fluid balance-based methods of quantifying fluid overload were valid in their look-back cohort of children undergoing continuous renal replacement therapy (CRRT).

Miscellanea

Carlesso et al. [84] analyzed, with the help of a mathematical model, the effect of diluting human plasma with crystalloid solutions that have strong ion difference (SID). Their findings were that the baseline bicarbonate concentration will determine the pH response to crystalloid infusion. Thus, if the crystalloid equals baseline bicarbonate concentration, pH will not be altered at constant PCO_2, whereas it decreases if the SID is grater and decreases if SID is lower than baseline bicarbonate.

In an observational study, Bonizzoli et al. [85] evaluated the rate of thrombosis associated with peripherally inserted central venous catheters (PICC) and central venous catheters in patients discharged from the ICU. Patients with PICC ($n = 114$) had a significantly higher incidence of deep venous thrombosis than patients with central venous catheters ($n = 125$) (27 vs. 10%), the majority of thrombosis occurring within 2 weeks after PICC insertion. Female gender and access through the left basilic vein were associated with a higher risk of thrombosis in the PICC group. The authors concluded that, in patients discharged from the ICU, routine ultrasound surveillance for the first 2 weeks after PICC insertion and preferential use of central venous catheters may be warranted.

De Keulenaer and coworkers [86] investigated whether intra-abdominal pressure (IAP) assessed by the urinary bladder pressure correlated well with femoral venous pressure in 149 critically ill, mechanically ventilated patients. The bias between IAP and femoral venous pressure was −1.5 and precision was 3.6 mmHg, with large limits of agreement (−8.6 and 5.7). When IAP was above 20 mmHg, bias was 0.7 with a precision of

2.0 mmHg (lower and upper limits of agreement of −3 and 4.6, respectively). Excluding patients with abdominal compartment syndrome, a femoral venous pressure of 11.5 mmHg predicted intra-abdominal hypertension with a sensitivity of 85% and a specificity of 67%. The authors' conclusions were that femoral venous pressure cannot be recommended as a surrogate measure for IAP measurement via the bladder, unless IAP is above 20 mmHg.

In a multicenter cohort study including data from 8,962 critically ill patients, Ho and coworkers [87] assessed whether the intensity of smoking history has a dose-related effect on hospital mortality. Smokers were more frequently male and had a higher incidence of severe chronic cardiovascular, respiratory and liver diseases. The risk of requiring mechanical ventilation and dying in hospital was higher and ICU stay was longer in smokers than in non-smokers. After adjusting for other confounders, intensity of smoking history (measured in pack-years) remained significantly associated with hospital mortality in a relatively linear fashion.

References

1. Villar J, Blanco J, Anon JM, Santos-Bouza A, Blanch L, Ambros A, Gandia F, Carriedo D, Mosteiro F, Basaldua S, Fernandez RL, Kacmarek RM (2011) The ALIEN study: incidence and outcome of acute respiratory distress syndrome in the era of lung protective ventilation. Intensive Care Med 37:1932–1941
2. Dellamonica J, Lerolle N, Sargentini C, Beduneau G, Di Marco F, Mercat A, Richard JC, Diehl JL, Mancebo J, Rouby JJ, Lu Q, Bernardin G, Brochard L (2011) PEEP-induced changes in lung volume in acute respiratory distress syndrome. Two methods to estimate alveolar recruitment. Intensive Care Med 37:1595–1604
3. Arnal JM, Paquet J, Wysocki M, Demory D, Donati S, Granier I, Corno G, Durand-Gasselin J (2011) Optimal duration of a sustained inflation recruitment maneuver in ARDS patients. Intensive Care Med 37:1588–1594
4. Marini JJ (2011) Recruitment by sustained inflation: time for a change. Intensive Care Med 37:1572–1574
5. Charron C, Bouferrache K, Caille V, Castro S, Aegerter P, Page B, Jardin F, Vieillard-Baron A (2011) Routine prone positioning in patients with severe ARDS: feasibility and impact on prognosis. Intensive Care Med 37:785–790
6. Mentzelopoulos SD, Theodoridou M, Malachias S, Sourlas S, Exarchos DN, Chondros D, Roussos C, Zakynthinos SG (2011) Scanographic comparison of high frequency oscillation with versus without tracheal gas insufflation in acute respiratory distress syndrome. Intensive Care Med 37:990–999
7. Nair P, Davies AR, Beca J, Bellomo R, Ellwood D, Forrest P, Jackson A, Pye R, Seppelt I, Sullivan E, Webb S (2011) Extracorporeal membrane oxygenation for severe ARDS in pregnant and postpartum women during the 2009 H1N1 pandemic. Intensive Care Med 37:648–654
8. Forrest P, Ratchford J, Burns B, Herkes R, Jackson A, Plunkett B, Torzillo P, Nair P, Granger E, Wilson M, Pye R (2011) Retrieval of critically ill adults using extracorporeal membrane oxygenation: an Australian experience. Intensive Care Med 37:824–830
9. Patroniti N, Zangrillo A, Pappalardo F, Peris A, Cianchi G, Braschi A, Iotti GA, Arcadipane A, Panarello G, Ranieri VM, Terragni P, Antonelli M, Gattinoni L, Oleari F, Pesenti A (2011) The Italian ECMO network experience during the 2009 influenza A(H1N1) pandemic: preparation for severe respiratory emergency outbreaks. Intensive Care Med 37:1447–1457
10. Costa R, Spinazzola G, Cipriani F, Ferrone G, Festa O, Arcangeli A, Antonelli M, Proietti R, Conti G (2011) A physiologic comparison of proportional assist ventilation with load-adjustable gain factors (PAV+) versus pressure support ventilation (PSV). Intensive Care Med 37:1494–1500
11. Roze H, Lafrikh A, Perrier V, Germain A, Dewitte A, Gomez F, Janvier G, Ouattara A (2011) Daily titration of neurally adjusted ventilatory assist using the diaphragm electrical activity. Intensive Care Med 37:1087–1094
12. Piquilloud L, Vignaux L, Bialais E, Roeseler J, Sottiaux T, Laterre PF, Jolliet P, Tassaux D (2011) Neurally adjusted ventilatory assist improves patient–ventilator interaction. Intensive Care Med 37:263–271
13. Tuchscherer D, Z'Graggen WJ, Passath C, Takala J, Sinderby C, Brander L (2011) Neurally adjusted ventilatory assist in patients with critical illness-associated polyneuromyopathy. Intensive Care Med 37:1951–1961
14. Zapata L, Vera P, Roglan A, Gich I, Ordonez-Llanos J, Betbese AJ (2011) B-type natriuretic peptides for prediction and diagnosis of weaning failure from cardiac origin. Intensive Care Med 37:477–485
15. Sellares J, Ferrer M, Cano E, Loureiro H, Valencia M, Torres A (2011) Predictors of prolonged weaning and survival during ventilator weaning in a respiratory ICU. Intensive Care Med 37:775–784
16. Laghi F (2011) Stratification of difficulty in weaning. Intensive Care Med 37:732–734
17. Fikkers BG, Staatsen M, van den Hoogen FJ, van der Hoeven JG (2011) Early and late outcome after single step dilatational tracheostomy versus the guide wire dilating forceps technique: a prospective randomized clinical trial. Intensive Care Med 37:1103–1109
18. Zanella A, Scaravilli V, Isgro S, Milan M, Cressoni M, Patroniti N, Fumagalli R, Pesenti A (2011) Fluid leakage across tracheal tube cuff, effect of different cuff material, shape, and positive expiratory pressure: a bench-top study. Intensive Care Med 37:343–347
19. Moran I, Cabello B, Manero E, Mancebo J (2011) Comparison of the effects of two humidifier systems on endotracheal tube resistance. Intensive Care Med 37:1773–1779
20. Sinha P, Flower O, Soni N (2011) Deadspace ventilation: a waste of breath! Intensive Care Med 37:735–746
21. Gancel PE, Roupie E, Guittet L, Laplume S, Terzi N (2011) Accuracy of a transcutaneous carbon dioxide pressure monitoring device in emergency room patients with acute respiratory failure. Intensive Care Med 37:348–351
22. Barwing J, Pedroni C, Quintel M, Moerer O (2011) Influence of body position, PEEP and intra-abdominal pressure on the catheter positioning for neurally adjusted ventilatory assist. Intensive Care Med 37:2041–2045

23. Demoule A, Morelot-Panzini C, Prodanovic H, Cracco C, Mayaux J, Duguet A, Similowski T (2011) Identification of prolonged phrenic nerve conduction time in the ICU: magnetic versus electrical stimulation. Intensive Care Med 37:1962–1968
24. Chiumello D, Gallazzi E, Marino A, Berto V, Mietto C, Cesana B, Gattinoni L (2011) A validation study of a new nasogastric polyfunctional catheter. Intensive Care Med 37:791–795
25. Spies C, Macguill M, Heymann A, Ganea C, Krahne D, Assman A, Kosiek HR, Scholtz K, Wernecke KD, Martin J (2011) A prospective, randomized, double-blind, multicenter study comparing remifentanil with fentanyl in mechanically ventilated patients. Intensive Care Med 37:469–476
26. Clouzeau B, Bui HN, Guilhon E, Grenouillet-Delacre M, Leger MS, Saghi T, Pillot J, Filloux B, Coz S, Boyer A, Vargas F, Gruson D, Hilbert G (2011) Fiberoptic bronchoscopy under noninvasive ventilation and propofol target-controlled infusion in hypoxemic patients. Intensive Care Med 37:1969–1975
27. Abreu SC, Antunes MA, Pelosi P, Morales MM, Rocco PR (2011) Mechanisms of cellular therapy in respiratory diseases. Intensive Care Med 37:1421–1431
28. Caironi P, Langer T, Carlesso E, Protti A, Gattinoni L (2011) Time to generate ventilator-induced lung injury among mammals with healthy lungs: a unifying hypothesis. Intensive Care Med 37:1913–1920
29. de Prost N, Saumon G, Dreyfuss D (2011) Modeling the time-course of ventilator-induced lung injury: what can we learn from interspecies discrepancies? Intensive Care Med 37:1901–1903
30. Fodil R, Lellouche F, Mancebo J, Sbirlea-Apiou G, Isabey D, Brochard L, Louis B (2011) Comparison of patient–ventilator interfaces based on their computerized effective dead space. Intensive Care Med 37:257–262
31. Cammarota G, Olivieri C, Costa R, Vaschetto R, Colombo D, Turucz E, Longhini F, Della Corte F, Conti G, Navalesi P (2011) Noninvasive ventilation through a helmet in postextubation hypoxemic patients: physiologic comparison between neurally adjusted ventilatory assist and pressure support ventilation. Intensive Care Med 37:1943–1950
32. Milan M, Zanella A, Isgro S, Deab SA, Magni F, Pesenti A, Patroniti N (2011) Performance of different continuous positive airway pressure helmets equipped with safety valves during failure of fresh gas supply. Intensive Care Med 37:1031–1035
33. Ducros L, Logeart D, Vicaut E, Henry P, Plaisance P, Collet JP, Broche C, Gueye P, Vergne M, Goetgheber D, Pennec PY, Belpomme V, Tartiere JM, Lagarde S, Placente M, Fievet ML, Montalescot G, Payen D (2011) CPAP for acute cardiogenic pulmonary oedema from out-of-hospital to cardiac intensive care unit: a randomised multicentre study. Intensive Care Med 37:1501–1509
34. Nouira S, Boukef R, Bouida W, Kerkeni W, Beltaief K, Boubaker H, Boudhib L, Grissa MH, Trimech MN, Boussarsar H, Methamem M, Marghli S, Ltaief M (2011) Non-invasive pressure support ventilation and CPAP in cardiogenic pulmonary edema: a multicenter randomized study in the emergency department. Intensive Care Med 37:249–256
35. L'Her E (2011) Is the noninvasive ventilatory mode of importance during cardiogenic pulmonary edema? Intensive Care Med 37:190–192
36. Cammarota G, Vaschetto R, Turucz E, Dellapiazza F, Colombo D, Blando C, Della Corte F, Maggiore SM, Navalesi P (2011) Influence of lung collapse distribution on the physiologic response to recruitment maneuvers during noninvasive continuous positive airway pressure. Intensive Care Med 37:1095–1102
37. Chiumello D, Chevallard G, Gregoretti C (2011) Non-invasive ventilation in postoperative patients: a systematic review. Intensive Care Med 37:918–929
38. Azoulay E, Demoule A, Jaber S, Kouatchet A, Meert AP, Papazian L, Brochard L (2011) Palliative noninvasive ventilation in patients with acute respiratory failure. Intensive Care Med 37:1250–1257
39. Dimassi S, Vargas F, Lyazidi A, Roche-Campo F, Dellamonica J, Brochard L (2011) Intrapulmonary percussive ventilation superimposed on spontaneous breathing: a physiological study in patients at risk for extubation failure. Intensive Care Med 37:1269–1276
40. de Graaff AE, Dongelmans DA, Binnekade JM, de Jonge E (2011) Clinicians' response to hyperoxia in ventilated patients in a Dutch ICU depends on the level of FiO_2. Intensive Care Med 37:46–51
41. Branson RD, Robinson BR (2011) Oxygen: when is more the enemy of good? Intensive Care Med 37:1–3
42. Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, Ricard JD (2011) Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med 37:1780–1786
43. Visser DY, Jansen NJ, Ijland MM, de Koning TJ, van Hasselt PM (2011) Intracranial bleeding due to vitamin K deficiency: advantages of using a pediatric intensive care registry. Intensive Care Med 37:1014–1020
44. Warrick C, Naik H, Avis S, Fletcher P, Franklin BD, Inwald D (2011) A clinical information system reduces medication errors in paediatric intensive care. Intensive Care Med 37:691–694
45. Brown KL, Pagel C, Pienaar A, Utley M (2011) The relationship between workload and medical staffing levels in a paediatric cardiac intensive care unit. Intensive Care Med 37:326–333
46. Latour JM, van Goudoever JB, Duivenvoorden HJ, Albers MJ, van Dam NA, Dullaart E, van Heerde M, de Neef M, Verlaat CW, van Vught EM, Hazelzet JA (2011) Construction and psychometric testing of the EMPATHIC questionnaire measuring parent satisfaction in the pediatric intensive care unit. Intensive Care Med 37:310–318
47. Latour JM, van Goudoever JB, Schuurman BE, Albers MJ, van Dam NA, Dullaart E, van Heerde M, Verlaat CW, van Vught EM, Hazelzet JA (2011) A qualitative study exploring the experiences of parents of children admitted to seven Dutch pediatric intensive care units. Intensive Care Med 37:319–325
48. Lopez-Herce J, Fernandez B, Urbano J, Mencia S, Solana MJ, Rodriguez-Nunez A, Bellon JM, Carrillo A (2011) Hemodynamic, respiratory, and perfusion parameters during asphyxia, resuscitation, and post-resuscitation in a pediatric model of cardiac arrest. Intensive Care Med 37:147–155
49. Botran M, Lopez-Herce J, Urbano J, Solana MJ, Garcia A, Carrillo A (2011) Chest compressions versus ventilation plus chest compressions: a randomized trial in a pediatric asphyxial cardiac arrest animal model. Intensive Care Med 37:1873–1880
50. Thiagarajan RR, Laussen PC, Rycus PT, Bartlett RH, Bratton SL (2007) Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. Circulation 116:1693–1700

51. Tajik M, Cardarelli MG (2008) Extracorporeal membrane oxygenation after cardiac arrest in children: what do we know? Eur J Cardiothorac Surg 33:409–417
52. Humpl T, Reyes JT, Erickson S, Armano R, Holtby H, Adatia I (2011) Sildenafil therapy for neonatal and childhood pulmonary hypertensive vascular disease. Cardiol Young 21:187–193
53. Shah PS, Ohlsson A (2011) Sildenafil for pulmonary hypertension in neonates. Cochrane Database Syst Rev (8):CD005494
54. Fraisse A, Butrous G, Taylor MB, Oakes M, Dilleen M, Wessel DL (2011) Intravenous sildenafil for postoperative pulmonary hypertension in children with congenital heart disease. Intensive Care Med 37:502–509
55. Hebbar KB, Stockwell JA, Fortenberry JD (2011) Clinical effects of adding fludrocortisone to a hydrocortisone-based shock protocol in hypotensive critically ill children. Intensive Care Med 37:518–524
56. Hebbar KB, Stockwell JA, Leong T, Fortenberry JD (2011) Incidence of adrenal insufficiency and impact of corticosteroid supplementation in critically ill children with systemic inflammatory syndrome and vasopressor-dependent shock. Crit Care Med 39:1145–1150
57. Kuhlwein E, Balmer C, Cannizzaro V, Frey B (2011) Determinants of arterial and central venous blood pressure variation in ventilated critically ill children. Intensive Care Med 37:118–123
58. Teng S, Kaufman J, Pan Z, Czaja A, Shockley H, da Cruz E (2011) Continuous arterial pressure waveform monitoring in pediatric cardiac transplant, cardiomyopathy and pulmonary hypertension patients. Intensive Care Med 37:1297–1301
59. Hockenhull JC, Dwan K, Boland A, Smith G, Bagust A, Dundar Y, Gamble C, McLeod C, Walley T, Dickson R (2008) The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation. Health Technology Assessment (Winchester, England) 12:iii–iv, xi–xii, 1–154
60. Miller MR, Niedner MF, Huskins WC, Colantuoni E, Yenokyan G, Moss M, Rice TB, Ridling D, Campbell D, Brilli RJ, National Association of Children's Hospitals and Related Institutions Pediatric Intensive Care Unit Central Line-Associated Bloodstream Infection Quality Transformation Teams (2011) Reducing PICU central line-associated bloodstream infections: 3-year results. Pediatrics 128:e1077–e1083
61. Niedner MF, Huskins WC, Colantuoni E, Muschelli J, Ii JM, Rice TB, Brilli RJ, Miller MR (2011) Epidemiology of central line-associated bloodstream infections in the pediatric intensive care unit. Infect Control Hosp Epidemiol 32:1200–1208
62. Rey C, Alvarez F, De-La-Rua V, Concha A, Medina A, Diaz JJ, Menendez S, Los-Arcos M, Mayordomo-Colunga J (2011) Intervention to reduce catheter-related bloodstream infections in a pediatric intensive care unit. Intensive Care Med 37:678–685
63. Roeleveld PP, Guijt D, Kuijper EJ, Hazekamp MG, de Wilde RB, de Jonge E (2011) Ventilator-associated pneumonia in children after cardiac surgery in the Netherlands. Intensive Care Med 37:1656–1663
64. Srinivasan R, Asselin J, Gildengorin G, Wiener-Kronish J, Flori HR (2009) A prospective study of ventilator-associated pneumonia in children. Pediatrics 123:1108–1115
65. Hall MW, Knatz NL, Vetterly C, Tomarello S, Wewers MD, Volk HD, Carcillo JA (2011) Immunoparalysis and nosocomial infection in children with multiple organ dysfunction syndrome. Intensive Care Med 37:525–532
66. Janssen NJ, Tan EY, Staal M, Janssen EP, Leroy PL, Lousberg R, van Os J, Schieveld JN (2011) On the utility of diagnostic instruments for pediatric delirium in critical illness: an evaluation of the Pediatric Anesthesia Emergence Delirium Scale, the Delirium Rating Scale 88, and the Delirium Rating Scale-Revised R-98. Intensive Care Med 37:1331–1337
67. Hoy SM, Keating GM (2011) Dexmedetomidine: a review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. Drugs 71:1481–1501
68. Czaja AS, Zimmerman JJ (2009) The use of dexmedetomidine in critically ill children. Pediatric Critical Care Medicine 10:381–386
69. Le KN, Moffett BS, Ocampo EC, Zaki J, Mossad EB (2011) Impact of dexmedetomidine on early extubation in pediatric cardiac surgical patients. Intensive Care Med 37:686–690
70. Tsapis M, Mignot C, Katsahian S, Arbaoui H, Ayachi A (2011) Case-control study of respiratory dynamic compliance in mechanically ventilated near-term newborns in a pre-hospital setting. Intensive Care Med 37:2008–2014
71. Cogo PE, Facco M, Simonato M, De Luca D, De Terlizi F, Rizzotti U, Verlato G, Bellagamba MP, Carnielli VP (2011) Pharmacokinetics and clinical predictors of surfactant redosing in respiratory distress syndrome. Intensive Care Med 37:510–517
72. Williams AM, Abramo TJ, Shah MV, Miller RA, Burney-Jones C, Rooks S, Estrada C, Arnold DH (2011) Safety and clinical findings of BiPAP utilization in children 20 kg or less for asthma exacerbations. Intensive Care Med 37:1338–1343
73. James CS, Hallewell CP, James DP, Wade A, Mok QQ (2011) Predicting the success of non-invasive ventilation in preventing intubation and re-intubation in the paediatric intensive care unit. Intensive Care Med 37:1994–2001
74. Piastra M, De Luca D, Marzano L, Stival E, Genovese O, Pietrini D, Conti G (2011) The number of failing organs predicts non-invasive ventilation failure in children with ALI/ARDS. Intensive Care Med 37:1510–1516
75. Mayordomo-Colunga J, Medina A, Rey C, Diaz JJ, Concha A, Los M, Menendez S (2009) Predictive factors of non invasive ventilation failure in critically ill children: a prospective epidemiological study. Intensive Care Med 35:527–536
76. Essouri S, Durand P, Chevret L, Balu L, Devictor D, Fauroux B, Tissieres P (2011) Optimal level of nasal continuous positive airway pressure in severe viral bronchiolitis. Intensive Care Med 37:2002–2007
77. Schibler A, Pham TM, Dunster KR, Foster K, Barlow A, Gibbons K, Hough JL (2011) Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med 37:847–852
78. De Luca D, Minucci A, Tripodi D, Piastra M, Pietrini D, Zuppi C, Conti G, Carnielli VP, Capoluongo E (2011) Role of distinct phospholipases A2 and their modulators in meconium aspiration syndrome in human neonates. Intensive Care Med 37:1158–1165
79. Lubrano R, Cecchetti C, Elli M, Tomasello C, Guido G, Di Nardo M, Masciangelo R, Pasotti E, Barbieri MA, Bellelli E, Pirozzi N (2011) Prognostic value of extravascular lung water index in critically ill children with acute respiratory failure. Intensive Care Med 37:124–131
80. Borik S, Simon AJ, Nevo-Caspi Y, Mishali D, Amariglio N, Rechavi G, Paret G (2011) Increased RNA editing in children with cyanotic congenital heart disease. Intensive Care Med 37:1664–1671

81. Nevo-Caspi Y, Amariglio N, Rechavi G, Paret G (2011) A-to-I RNA editing is induced upon hypoxia. Shock 35:585–589
82. Hill H, Baines P, Barton P, Newland P, Terlouw D, Turner M (2011) Uncertainties in the measurement of blood glucose in paediatric intensive care: implications for clinical trials of tight glycaemic control. Intensive Care Med 37:1517–1524
83. Selewski DT, Cornell TT, Lombel RM, Blatt NB, Han YY, Mottes T, Kommareddi M, Kershaw DB, Shanley TP, Heung M (2011) Weight-based determination of fluid overload status and mortality in pediatric intensive care unit patients requiring continuous renal replacement therapy. Intensive Care Med 37:1166–1173
84. Carlesso E, Maiocchi G, Tallarini F, Polli F, Valenza F, Cadringher P, Gattinoni L (2011) The rule regulating pH changes during crystalloid infusion. Intensive Care Med 37:461–468
85. Bonizzoli M, Batacchi S, Cianchi G, Zagli G, Lapi F, Tucci V, Martini G, Di Valvasone S, Peris A (2011) Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. Intensive Care Med 37:284–289
86. De Keulenaer BL, Regli A, Dabrowski W, Kaloiani V, Bodnar Z, Cea JI, Litvin AA, Davis WA, Palermo AM, De Waele JJ, Malbrain ML (2011) Does femoral venous pressure measurement correlate well with intrabladder pressure measurement? A multicenter observational trial. Intensive Care Med 37:1620–1627
87. Ho KM, Hart G, Austin D, Hunter M, Botha J, Chavan S (2011) Dose-related effect of smoking on mortality in critically ill patients: a multicentre cohort study. Intensive Care Med 37:981–989