

Peter Andrews
Elie Azoulay
Massimo Antonelli
Laurent Brochard
Christian Brun-Buisson
Daniel De Backer
Geoffrey Dobb
Jean-Yves Fagon
Herwig Gerlach
Johan Groeneveld
Duncan Macrae
Jordi Mancebo
Philipp Metnitz
Stefano Nava
Jerôme Pugin
Michael Pinsky
Peter Radermacher
Christian Richard

Year in Review in Intensive Care Medicine, 2006. III. Circulation, ethics, cancer, outcome, education, nutrition, and pediatric and neonatal critical care

Received: 22 January 2007
Accepted: 22 January 2007
Published online: 14 February 2007
© Springer-Verlag 2007

This review intends to summarize all articles published in Intensive Care Medicine in 2006, grouped by specific topics

P. Andrews
Western General Hospital, Intensive Care
Medicine Unit,
Edinburgh, UK

E. Azoulay
Saint Louis Hospital, Intensive Care
Medicine Unit,
Paris, France

M. Antonelli
Universita Cattolica del Sacre Cuore,
Department of Intensive Care and
Anesthesiology,
Rome, Italy

L. Brochard (✉)
AP-HP, Hôpital Henri Mondor, Université
Paris 12, Réanimation Médicale, INSERM
U 651,
94000 Créteil, France
e-mail: laurent.brochard@hmn.aphp.fr
Tel.: +33-1-49812545
Fax: +33-1-42079943

C. Brun-Buisson
AP-HP, Hôpital Henri Mondor, Université
Paris 12, Réanimation Médicale,
Créteil, France

D. De Backer
Erasmus Hospital, Service des Soins
Intensifs,
Brussels, Belgium

G. Dobb
Royal Perth Hospital, Intensive Care
Medicine Unit,
Perth, Australia

J.-Y. Fagon
European Georges Pompidou Hospital,
Intensive Care Medicine Unit,
Paris, France

H. Gerlach
Vivantes-Klinikum Neukoelln, Department
of Anesthesiology,
Berlin, Germany

J. Groeneveld
VUMC, Intensive Care Medicine Unit,
Amsterdam, The Netherlands

D. Macrae
Royal Brompton Hospital, Pediatric
Intensive Care Unit,
London, UK

J. Mancebo
Hospital Sant Pau, Intensive Care Medicine
Unit,
Barcelona, Spain

P. Metnitz
University Hospital of Vienna, Department
of Anesthesia and General Intensive Care
Medicine,
Vienna, Austria

S. Nava
Fondazione S. Maugeri, Intensive Care
Medicine Unit,
Pavia, Italy

J. Pugin
University Hospital of Geneva, Intensive
Care Medicine Unit,
Geneva, Switzerland

M. Pinsky
University of Pittsburgh Medical Center,
Intensive Care Medicine Unit,
Pittsburgh Pennsylvania, USA

P. Radermacher
University Medical School of Ulm,
Department of Anesthesia,
Ulm, Germany

C. Richard
University Hospital of Le Kremlin-Bicetre,
Intensive Care Unit,
Le Kremlin-Bicetre, France

Circulation

Evaluation of the microcirculation

Microcirculation has become a major topic of interest. Several studies have shown that microcirculatory alterations frequently occur in patients with septic shock, and that these alterations are correlated with the development of organ failure and death. Although direct visualization is now feasible, indirect measurements are more commonly used at the bedside. Among the indirect measurements, measurements of tissue carbon dioxide pressure can be used. These measurements can be obtained non-invasively either in the stomach (gastric tonometry) or in the sublingual area. Creteur et al. [1] investigated in 18 patients with septic shock the relationship between sublingual microvascular perfusion, assessed using an orthogonal polarization spectral imaging device, and sublingual and gastric carbon dioxide pressure. They observed an inverse relationship between microvascular perfusion and sublingual to arterial carbon dioxide pressure gap. Dobutamine administration, at a dose of $5 \mu\text{g}/\text{kg min}^{-1}$, increased microvascular perfusion and decreased sublingual carbon dioxide. In addition, measurements of carbon dioxide pressure in the gastric and sublingual areas were highly related. These findings suggest that regional microcirculatory flow is the main determinant of sublingual carbon dioxide pressure. In addition, these findings suggest that the sublingual area can be used as a surrogate of other microvascular beds, including the splanchnic area. The accompanying editorial by Ince [2] discussed the determinants of a raised tissue carbon dioxide pressure. Although mitochondrial dysfunction may be evoked, the inverse relationship between perfusion and carbon dioxide pressure suggest that the altered flow, rather than mitochondrial dysfunction, was responsible for the elevated carbon dioxide.

Increased permeability and local dysoxia may also be related to microvascular alterations. In 9 patients with septic shock and 7 patients with severe sepsis, Jorgensen et al. [3] evaluated the colorectal permeability and local dysoxia. A homemade microdialysis probe was inserted in the rectum to measure rectal lactate production and calculation of rectal to blood lactate gradient as a marker of local dysoxia. Intestinal permeability was assessed using isotopic substances, by rectal infusion of $^{99\text{m}}\text{Tc}$ -DTPA and evaluation of cumulative recovery of this substance in the plasma at 1 h. Colorectal permeability was increased in sepsis, and especially in patients with septic shock. Similarly, lactate levels and lactate gradients were increased in patients with septic shock and in patients with severe sepsis. The severity of permeability alterations was correlated with lactate gradients. These results suggest that gut permeability alterations and local dysoxia occur in the large intestine. Although there is no proof of a cause-and-effect mechanism, it is likely that

both were sharing a common cause, and microcirculatory alterations may be one of these causes.

A place for echocardiography?

The echocardiographic evaluation of the patient in circulatory failure is now feasible, both by trans-thoracic and trans-esophageal route. Cardiac output, indices of left and right ventricular dysfunction, intravascular pressure and volumes, and indices of fluid responsiveness can be measured; however, the acquisition of some of these indices may require a large experience in echocardiography. Vieillard-Baron et al. [4] focused their attention on four indices obtained by trans-esophageal echocardiography that may be sufficient to evaluate right and left ventricular function and fluid responsiveness: left ventricular ejection fraction; right ventricular end-diastolic area and detection of paradoxical septum motion; and respiratory changes in superior vena cava diameter. These indices were either quantified by full-trained investigators or qualitatively assessed (normal, moderately altered, severely altered) by intensivists trained in echocardiography. Eighty-three evaluations were performed in 30 patients in septic shock, and a very satisfactory agreement between qualitative and quantitative assessment was observed. These results suggest that intensivists with a minimal echocardiographic training can rapidly categorize cardiovascular dysfunction in patients with septic shock. This qualitative analysis can be obtained within a couple of minutes. Although monitoring will still be intermittent, rapid and repeated analysis of the cardiovascular function by is now feasible.

Treatment of hemodynamic alterations

Decreased vascular tone is a key finding in patients with septic shock. Vasopressor agents are used to correct hypotension and adrenergic agents are classically used for this purpose. Among these agents, norepinephrine is one of the most potent and one of the most commonly used; however, adrenergic compounds are pro-arrhythmic, have metabolic and immunologic effects. In addition, septic patients often present with resistance to adrenergic agents, which usually, but not always, can be overcome by an increase in norepinephrine dosages. Vasopressin deficiency seems to occur in patients with septic shock and arginine vasopressin administration may be an alternative to norepinephrine; however, concerns were raised on the safety of vasopressin, which may impair splanchnic perfusion. Lauzier et al. [5] conducted a small ($n = 23$) randomized study to compare the effectiveness and safety of norepinephrine and arginine vasopressin in the therapy of early septic shock (< 12 h of duration). Patients were randomized to receive either drug as the sole vasopressor agent; accordingly, very high doses (higher

than usually recommended) of vasopressin were used (up to 0.20 U/min). In one-third of the patients treated with vasopressin, the maximal dose of vasopressin was insufficient to restore blood pressure and norepinephrine had to be added. Vasopressin improved renal function compared with norepinephrine. Splanchnic perfusion, evaluated using gastric tonometry, was not affected by norepinephrine or vasopressin. One patient treated with vasopressin developed myocardial ischemia. Although this study was limited by the very small sample size, it suggests that vasopressin may be an excellent alternative to norepinephrine; however, the safety of high doses of vasopressin can be questioned, as illustrated by the development of myocardial ischemia.

Factors promoting hemodynamic alterations

Reperfusion injury is frequently observed in organ transplantation and is associated with microvascular dysfunction, vascular permeability, cellular necrosis and organ dysfunction. Although pathophysiologic mechanisms are multiple, the implication of inflammation and coagulation processes has been demonstrated in experimental conditions. Cottini et al. [6] evaluated in a retrospective study the factors associated with the development of reperfusion injury in 60 patients after lung transplant. As expected, lung reperfusion syndrome was associated with a longer period of mechanical ventilation and a higher ICU mortality. Several factors were independently associated with the development of reperfusion injury: the presence of pulmonary hypertension in native lungs; pulmonary hypertension in the immediate post-transplantation period and its persistence during the first 48 h, bleeding and difficult hemostasis during surgery, and requirement for adrenergic support during the first 48 h. These associations do not provide insight into the mechanisms leading to reperfusion injury in lung transplantation; however, identifying risks factors associated with reperfusion injury may be useful, both for triage of patients and for implementation of early interventions aimed at limiting the consequences of reperfusion injury.

Ethics in the ICU

Several aspects of ethics in the ICU were addressed in the journal in 2006, namely, satisfaction of family members, end-of-life practices as reported by nurses and by emergency physicians, and the ethics of critical care research.

End-of-life decisions

Critical care nurses play a pivotal role in end-of-life care in the ICU. The role of European intensive care nurses in end-

of-life decision making was compared across 17 European countries by a collaborative group from the Ethics Section of the European Society of Intensive Care Medicine (the Ethicus study) [7]. Physicians perceived nurses as involved to a large extent in end-of-life decisions, but not as initiating the discussion. Strikingly, the level of perceived participation varied across different regions. In the editorial accompanying this paper, Curtis and Shannon highlighted the importance of interdisciplinary communication and collaboration to determine the goals of care [8]. Encouragement for more qualitative studies to examine the quality of collaborative decision making from the perspective of physicians, nurses, and families were particularly encouraged. Another aspect of end-of-life care was depicted by Ferrand and Marty in a survey where 1,069 emergency physicians working in 192 French emergency mobile units were asked to complete a 40-item questionnaire about most recent end-of-life decision in the prehospital setting [9]. The main result from this study was that treatment withholding and withdrawal was common in the prehospital setting in France (76.3% of the answering physicians), and even though decisions are made for patients by physicians they have not met before, patients or relatives wishes were frequently not known, and in 45% of the cases, the end-of-life decision was not discussed with other physicians. Factors independently associated with prehospital withdrawal decision included multiple trauma, intubation, chronic disease with severe heart failure, acute event with postanoxic coma, emergency physician from a teaching hospital, male patient, and no sedation. In the accompanying editorial, Rocker reminds us that we all need to be wary of decisions made in haste that cannot be undone, and provides evidence from literature that determinants of end-of-life decisions may be subjective [10]. Rocker concludes that in the emergency room or prehospital setting, broader consultation and less hasty decision making based on any health care provider's perception of "imminent death or futility" are needed to prevent errors in judgment.

Informed consent

Three studies on informed consent in critical care research were published in the journal in 2006. Chenaud and colleagues performed a prospective observational study to analyze the procedure of informed consent for ICU research obtained before ICU admission [11]. Data were obtained from 36 cardiac surgery patients who accepted to participate in a coagulation study. Information on the study included an oral presentation of the coagulation study and an informative leaflet the day before surgery on the ward. The finding that 22% of the patients did not know they had participated in a study and 25% of the patients could not recall the study purpose and the related risk raises logically the question of the ethical value of informed consent in this

setting. In most European countries, emergency research is now possible with a delayed consent, or a mere waiver. In a prospective observational study in three Dutch ICUs Veelo et al. reported the impact of a change in the Dutch Directive on Medical Research Involving Human Subjects on the number of eligible ICU patients for medical research [12]. The new directive allows family members to act as legal representatives for granting consent/assent in case the patient is himself incapacitated, when the previous legislation restricted that possibility only to the spouse. The change in the Dutch Directive has increased the number of surrogates allowed to give informed consent. Representatives felt very confident in their ability to represent the patients. In turn, patients were equally confident that their representatives were able to represent them. An assessment of the impact of the European Directive for clinical research 2 years after its implementation was provided in the same issue of the journal [13]. A third study on informed consent in ICU clinical trials sought to identify the proportion of critically ill patients able to consent to participation in a randomized controlled trial (RCT) and to assess to what extent patient consent and relative assent processes could be conducted according to ethics committee permissions [14]. From data collected during the PAC-man study published earlier, only 2.6% of the patients were able to consent before randomization, and only one-third of the patients could provide consent retrospectively. Again, this study demonstrates difficulties experienced in obtaining consent from critically ill patients to participate in medical research and raises important issues about the ethical basis of the consent process in critical care. In the accompanying editorial, Lemaire pointed out the thorough description of each step of the consent process, including the need for an authorization to use the data from a central national ethics board if the patient dies or never regains consciousness [15]. Lemaire acknowledged that most legislations of EU member states have recognized that the family is the “natural” legal representative of any incompetent patient, even when they tried to propose a system by which any person could designate in advance his chosen representative, which in fact they rarely do. In the study by Harvey et al., the fact that when patients regained mental competence they overwhelmingly confirmed the decision made earlier on their behalf is obviously a major finding.

Cancer patients

In a prospective study, Rego Lins Fumis and colleagues evaluated the determinants of satisfaction in 164 relatives of critically ill cancer patients [16]. Beside the fact that this is the first study focusing specifically on this patient population, its finding emphasizes the need for improving communication skills with patients’ relatives, more specifically regarding information on the prognosis.

Benoit and colleagues reported outcomes in 37 critically ill cancer patients requiring cancer chemotherapy along with life-sustaining support in the ICU or ICU monitoring [17]. Most patients had a high-grade malignancy and 30% a relapsing disease. In 41% of the cases, a clinically or microbiologically infection was documented; 62% received mechanical ventilation and 24% dialysis. Mortality was associated with the need for mechanical ventilation, for instance, hospital mortality was 14% in non-ventilated patients and 61% in ventilated patients. The authors concluded that starting chemotherapy in the ICU for a life-threatening malignancy-related complication can be lifesaving even when infection or organ failure is present. As pointed out in the editorial from Azoulay and Afessa, improvements have been observed in the prognosis of cancer patients admitted to the ICU, based on patient selection, advances in the understanding of the pathophysiology of certain complications, and the use of non-invasive diagnostic and therapeutic strategies [18]. All these arguments represent a plea for changing our admission criteria in cancer patients requiring life-sustaining therapies.

Post ICU and long-term outcome

In an observational cohort study, Walsh and colleagues documented that, in ICUs that use restrictive transfusion triggers, up to 80% of the patients had anemia during and at ICU discharge [19]. The impact of anemia on functional recovery after intensive care requires investigation. In an observational cohort study in a single center, Walsh and colleagues documented the prevalence of anaemia among ICU survivors at the time of discharge home [20]. Again, about 80% of the ICU survivors were anaemic, and this persisted until hospital discharge.

Long-term outcomes and quality of life have been sought in ICU survivors in two prospective observational studies. In a single-center study, Griffiths et al. determined the incidence of sexual dysfunction in 127 patients in their first year after hospital discharge using a self-report measure [21]. Symptoms of sexual dysfunction were retrieved in 43.6% of the patients recovering from critical illness and appeared to be significantly associated with the presence of post-traumatic stress disorder symptomatology. In another prospective cohort study, Scales and colleagues compared estimates of pre-morbid health-related quality of life obtained 3 months after ICU discharge from 46 survivors of the acute respiratory distress syndrome (ARDS) with those of their substitute decision makers (at study entry) using the Short Form 36 (SF-36) [22]. Agreement between patients and their substitute decision makers was poor for all SF-36 components and differences reached significance in three domains. Compared with survivors, proxies tended to underestimate pre-morbid HRQOL. Patient age was

associated with the mean difference between estimates for the “Mental Health” domain. In the accompanying editorial, Granja and Azevedo underlined the major outcome information provided by HRQOL measurement and how decision making in critical care patients became highly influenced by the appreciation of patients’ future HRQOL [23].

Education

One of the activities of the European Society of Intensive Care Medicine regarding training in Intensive Care was reported in the journal: a 3-year project to develop an internationally acceptable competency-based training program in intensive care medicine for Europe [24]. The aim of the study was to define the core (minimum) competencies required of a specialist in adult intensive care medicine. A nominal group of 12 clinicians met in plenary session to rate the importance of the competence statements, constructed from over 5,250 suggestions from 57 countries, obtained by using online and postal surveys. Using consensus techniques (modified Delphi and nominal group) to enable interested stakeholders to identify and prioritize core competencies, 102 competence statements were generated, divided into 12 domains, which are internationally applicable but still able to accommodate local requirements. These results provide the foundation to build an international competency-based training program for intensive care medicine, and represents an important step toward the homogenization of the European educational structure.

Nutrition

The importance of nutrition to the outcome for critically ill patients is now well recognized, but many questions remain. Complications occur from both over and under feeding. To assess the effect of recent Consensus recommendations [25] for energy requirements in critically ill patients across a range of body mass index (BMI), Zauner and colleagues [26] measured resting energy expenditure (REE) using indirect calorimetry. This was compared with the Consensus recommendations of 25 kcal/kg total body weight and also estimates obtained from the Harris–Benedict equations and an estimate using ideal body weight at 25 kcal/kg. The 100 patients recruited had BMIs in the ranges 18.5–24.9 kg/m² (*n* = 47), 25–29.9 kg/m² (*n* = 35), 30–34.9 kg/m² (*n* = 10), and ≥ 35 kg/m² (*n* = 8). The average measured REE in the BMI groups was 24.8, 22, 20.4 and 16.3 kcal/kg, respectively. As seen in other studies the Harris–Benedict equation underestimated REE in critically ill patients and substitution of ideal body weight for actual body weight underestimated REE in obese patients. In short, the Consensus recommendations

of 25 kcal/kg provides a reasonable estimate for patients of normal BMI but becomes increasingly an overestimate as BMI increases. The authors conclude a different approach is needed for the increasing numbers of obese patients.

The evidence favoring use of enteral nutrition (EN) over parenteral nutrition (PN) comes mainly from studies in elective surgical or trauma patients. A multicenter, randomized, unblinded clinical trial comparing early PN with early “immune enhanced” EN in a heterogeneous population of critically ill patients was coordinated by the Italian Group for the Evaluation of Interventions in Intensive Care Medicine [27]. Total enrollment of 326 patients included 287 without severe sepsis or septic shock at study entry. An earlier interim analysis of the patients with severe sepsis or septic shock had shown an excess mortality in those randomized to early “immune enhanced” EN [28], after which such patients were excluded from the trial. Mortality at 28 days was similar in both EN and PN groups: overall 15.6 vs. 15.1%, and 12 vs. 13.8% in patients without severe sepsis; however, patients without severe sepsis at study entry had fewer episodes of severe sepsis or septic shock during their ICU stay, i.e., 7 vs. 19 (*p* = 0.022) and a significantly shorter ICU stay: 17.6 vs. 21.6 days. It is concluded that PN should be avoided if EN is possible, even at a low initial intake, but the authors do not advocate “immune enhanced” EN pending conclusive evidence of any benefit.

Gastro-intestinal transit

One of the major impediments to early EN is slow gastric emptying. Gastroparesis is known to be associated with both type-I and type-II diabetes mellitus. Nguyen and others [29] hypothesized that gastric emptying would be slower in critically ill patients with diabetes mellitus than without. [¹³C] octanoic acid breath tests were used to assess gastric emptying. Twelve critically ill type-II diabetics were age- and gender matched with 15 non-diabetics. Other patient characteristics, such as illness severity assessed by APACHE-II score on the study day, as well as use of sedation or analgesia, were also similar. Surprisingly, gastric emptying was quicker in the diabetics than the matched non-diabetics (or a cohort of unmatched non-diabetics) and similar to that in healthy volunteers. While the results might have been an aberration caused by the relatively small number of patients studied, the authors cite significant variability in proximal gastric motor function in diabetics, with some having accelerated liquid gastric emptying. When gastric emptying is severely impaired, a post-pyloric feeding tube provides a route to establish EN, but placement can be difficult in patients with gastric ileus unless endoscopy or radiological guidance are used. Lee and colleagues [30] conducted an open study in 20 consecutive ventilated patients to assess

the efficacy of a fixed protocol for placing post-pyloric feeding tubes. Ten minutes after 10 mg metoclopramide intravenously, a 140-cm 8-F fine-bore feeding tube was advanced through a nostril into the stomach (confirmed by acidic aspirate), and then in 5-cm increments as long as no resistance was felt. When resistance occurred the tube was withdrawn 5 cm. The tube was advanced to 95–105 cm, but if this had not occurred after 20 min, 200 ml of air was insufflated into the stomach and then further attempts were made to insert it. In 18 of 20 cases post-pyloric placement was achieved at the first attempt with four requiring gastric air insufflation. The authors concluded that this technique is effective in critically ill patients (detailed protocol appended to article).

Both constipation and diarrhea are common in critically ill patients. To determine the influence of severity of illness, medication, and selective decontamination or defecation, van der Spoel and others [31] studied a cohort of 50 consecutive mechanically ventilated patients who stayed in the ICU for at least 7 days. Enteral nutrition was started within 48 h, using a duodenal feeding tube when necessary and giving lactulose 30 ml tid if no stool was passed after 3–4 days and enemas at physician discretion. Six patients were excluded because of recent gastrointestinal surgery or short bowel syndrome. The median time to passage of stool was 6 days (mean SD 6.2 ± 2.5 days). Twenty-one patients received an enema a mean of 4.7 days after admission; diarrhea occurred at least once in 27, usually after the lactulose. Illness severity, assessed by APACHE-II score, and use of selective bowel decontamination did not affect defecation, but a delay in defecation was associated with greater use of vasoactive medication and higher SOFA scores.

Jaundice

To assess the frequency of collateral jaundice, defined as a serum bilirubin ≥ 2 mg/dl lasting for at least 48 h, in a heterogeneous population of ICU patients, Brienza and colleagues [32] measured bilirubin concentration in all patients for 6 months. Patients were excluded if the ICU stay was less than 48 h or if they had acute or chronic liver disease. In their cohort of 141 patients, 44 had “jaundice” (31.2%). In multivariate analysis, risk factors for “jaundice” were severe shock, sepsis, mechanical ventilation with PEEP ≥ 5 cm H₂O, and major surgery. Interestingly, no relationship was found between use of drugs regarded as hepatotoxic and the occurrence of jaundice, perhaps reflecting the low frequency of such events. A trend towards higher mortality in patients with “jaundice” did not reach conventional statistical significance ($p = 0.08$) except in patients with severe shock ($p = 0.03$) and patients after major surgery ($p = 0.01$).

Pediatric and neonatal critical care

Intensive Care Medicine has had another successful year in presenting new knowledge and comment to the pediatric and neonatal critical care community.

Ethical aspects of practice

The journal seeks to reflect a wide range of opinion, and to encourage debate in its editorial and correspondence page where findings or opinions are controversial. Provoost et al. [33] presented the results of a survey and expert review of the use of drugs with life-shortening effects in neonates and infants. Of the 253 live-born infants who died over a 1-year period and for whom information was available, drugs were administered directly before death in 57 (22.5%) cases. They found that physicians appear to be mistaken about the consequences of their actions, with some babies receiving lethal doses of drugs when the intention was only to relieve pain and distress, whereas other babies in whom it was intended to hasten death received doses of drugs judged unlikely to achieve this objective. In an accompanying editorial Truog [34] discussed the ethical paradigm of the “doctrine of double intent” and its relevance to end-of-life care in pediatric and neonatal critical care practice, pointing out that euthanasia is unlawful in most countries, with the notable exceptions of Belgium and The Netherlands. The ethics of pediatric practice were also discussed in a thoughtful editorial on the dilemma facing practitioners faced with treating babies with spinal muscular atrophy with respiratory disease (SMARD) [35]. The author pointed out that many European pediatricians are dubious about the rightness of tracheostomy in children with SMARD, as Giannini et al. [36] reported in two cases.

Mechanical ventilation and respiratory support

It is notoriously difficult to acquire information about the distribution of ventilation in neonates and children. Heinrich et al. [37] reported their use of a non-invasive technique, electrical impedance tomography (EIT), to determine the spatial distribution of ventilation in both ventilated and spontaneously breathing neonates. In an associated editorial, Wolf and Arnold [38], while welcoming the move of EIT from laboratory to bedside, pointed out that many relevant questions remain to be answered before EIT can be relied upon to provide clinicians with online information on lung recruitment and distribution of ventilation.

As in adults, studies continue to present information on new modes of respiratory support. Zaramella et al. [39]

reported the effects of a CPAP delivered by a conventional infant flow driver and CPAP delivered by a newly designed helmet on cerebral blood flow (CBF). Although the respiratory effects seemed equivalent, CBF was lower when the helmet device was used. This finding emphasizes the need to carefully assess extra-pulmonary as well as pulmonary effects of new respiratory technologies. Further studies will clearly be required before the safety of this particular device can be established. Lindwall et al. [40] also addressed a safety issue in their report of workplace NO and NO₂ concentrations in and around neonatal incubators during inhaled nitric oxide therapy in conjunction with nasal CPAP. Reassuringly, they concluded that neither 8-h time-weighted average nor 15-min short-term exposure limits were exceeded during normal operation or with a simulated accident. Two more papers explored new approaches to the ventilation of pre-term neonates. In a small randomized cross-over study, Hummler et al. [41] explored whether ventilation with volume-controlled SIMV (VC-SIMV) might lead to fewer episodes of desaturation than “conventional” pressure-controlled SIMV. Their findings are interesting in that, although they determined that tidal volume was better maintained with VC-SIMV, the duration of significant hypoxemia (defined as an SpO₂ < 80%) was not reduced, and conversely, the incidence of bradycardias was higher with VC-SIMV. In another study by Herber-Jonat et al. [42], infants were ventilated with pressure-assisted ventilation using a newly developed adaptive backup support mode, with and without pulse-oximetry-guided operation (SpO₂-sensitive backup). The authors reported that SpO₂-sensitive adaptive backup appeared to be safe and effective in reducing the incidence and duration of oxygen desaturation in this short-term trial. Finally, Manna et al. [43] reported on their use of flexible bronchoscopy in selected patients in their pediatric ICU. New information which explained the child’s clinical condition or influenced management was elicited in (76%) bronchoscopies.

Clinical treatment

Boluyt et al. [44] reported on the process undertaken in The Netherlands to develop recommendations for resuscitation of critically ill neonates and children with hypovolemia. The guideline was developed by a rigorous process which included detailed literature review, consultation, and peer review. The recommendation resulting from this process was that the first-choice fluid for resuscitation of neonates and children with hypovolemia is isotonic saline. In an editorial in the same issue of the journal, Carcillo and Tasker [45] review the history of fluid resuscitation using seminal studies as waypoints (recommended reading for all intensive care and pediatric trainees).

Two papers and an editorial are related to the important problem of phrenic nerve injury resulting in diaphragmatic

paralysis as a complication of cardiac surgery [46, 47, 48]. Lemmer et al. [46] reported on the clinical impact of diaphragmatic paralysis in a series of 74 children, concluding that early spontaneous recovery is rare and transthoracic plication of the paralyzed hemidiaphragm is effective. Dagan et al. [47] described the clinical course of bilateral diaphragmatic paralysis in 9 children in whom clinical recovery occurred within 7 weeks. Issues of diagnosis, influence on outcome, causation, prevention, and management were discussed by Ross-Russell in the accompanying editorial [49].

A number of reports focussed on general aspects of pediatric intensive care. Lopez-Herce et al. [50] described the successful application of transpyloric enteral nutrition in a large series of critically ill children. Although the overall rate of complications was small, complications were more frequent in the 53 children with renal failure in whom 56.6% required parenteral nutrition, compared with only 17.5% of the 420 without renal failure. The need to have a robust surveillance and infection control policy in pediatric critical care units was stressed by Katragkou et al. [51] who reported that the use of aminoglycosides appeared to be an independent risk factor in the acquisition of imipenem-resistant *Acinetobacter baumannii*.

The interpretation of acid-base status in the face of hyperchloremia is not well understood. Taylor et al. [52] reported that correcting for chloride using the principles of Stewart’s physicochemical theory produced a dramatic improvement in the relationship between anion gap, base deficit, and bicarbonate during treatment of children with diabetic ketoacidosis. They concluded that their simple bedside tool may be a useful adjunct to guide therapeutic interventions.

Morris et al. [53] published a report of a national survey from the UK on monitoring and management of children with traumatic brain injury. Only 59% of 127 children presenting in the emergency room with a Glasgow Coma Score of 8 or below received ICP monitoring and ICP targets, and other therapies varied widely. They concluded that there is an urgent need for greater standardization of practice founded on the increasingly secure evidence base in this field. It is interesting to reflect that while it may be relatively easy to produce peer-evaluated guidance, implementation by units or individual clinicians is in many instances highly variable (an area worthy of greater focus).

Sepsis and inflammation

Although there is much in common in the pathogenesis, detection, and management of sepsis across age range, it is widely recognized that neonates and children require different approaches [54]. Stephens et al. [55], investigating the possible role of endotoxin in triggering SIRS, showed that PICU patients developing SIRS had significantly lower serum IgG antitoxin core antibodies than those who

did not develop SIRS. The paper was accompanied by an editorial from Carcillo [56] which neatly encapsulated much of the current science surrounding the pathogenesis of SIRS. In a small study, Celebi et al. [49] evaluated the utility of procalcitonin and C-reactive protein as markers of inflammation and predictors of organ failure after pediatric cardiac surgery, concluding that peak PCT levels were highly predictive of mortality and organ failure, whereas CRP levels were not. This study must

be interpreted in the context of other recent publications comparing CRP and PCT as marker of inflammation [57]. The differences between pediatric critical care practice in the developed and developing world was highlighted in the report of Khilnani et al. [58]. They stressed the importance of falciparum malaria, fulminant hepatic failure, and dengue shock syndrome in addition to “traditional” causes of multiple organ dysfunction syndrome in their Indian PICU.

References

- Creteur J, De Backer D, Sakr Y, Koch M, Vincent JL (2006) Sublingual capnometry tracks microcirculatory changes in septic patients. *Intensive Care Med* 32:516–523
- Ince C (2006) Go with the flow-recruit the microcirculation! *Intensive Care Med* 32:488–489
- Jorgensen VL, Nielsen SL, Espersen K, Perner A (2006) Increased colorectal permeability in patients with severe sepsis and septic shock. *Intensive Care Med* 32:1790–1796
- Vieillard-Baron A, Charron C, Chergui K, Peyrouset O, Jardin F (2006) Bedside echocardiographic evaluation of hemodynamics in sepsis: Is a qualitative evaluation sufficient? *Intensive Care Med* 32:1547–1552
- Lauzier F, Levy B, Lamarre P, Lesur O (2006) Vasopressin or norepinephrine in early hyperdynamic septic shock: a randomized clinical trial. *Intensive Care Med* 32:1782–1789
- Cottini SR, Lerch N, de Perrot M, Treggiari MM, Spiliopoulos A, Nicod L, Ricou B (2006) Risk factors for reperfusion injury after lung transplantation. *Intensive Care Med* 32:557–563
- Benbenishty J, Ganz FD, Lippert A, Bulow HH, Wennberg E, Henderson B, Svantesson M, Baras M, Phelan D, Maia P, Sprung CL (2006) Nurse involvement in end-of-life decision making: the ETHICUS Study. *Intensive Care Med* 32:129–132
- Curtis JR, Shannon SE (2006) Transcending the silos: toward an interdisciplinary approach to end-of-life care in the ICU. *Intensive Care Med* 32:15–17
- Ferrand E, Marty J (2006) Prehospital withholding and withdrawal of life-sustaining treatments. The French LATASAMU Survey. *Intensive Care Med* 32:1498–1505
- Rocker G (2006) Life-support limitation in the pre-hospital setting. *Intensive Care Med* 32:1464–1466
- Chenaud C, Merlani P, Ricou B (2006) Informed consent for research in ICU obtained before ICU admission. *Intensive Care Med* 32:439–444
- Veelo DP, Spronk PE, Kuiper MA, Korevaar JC, van der Voort PH, Schultz MJ (2006) A change in the Dutch Directive on Medical Research Involving Human Subjects strongly increases the number of eligible intensive care patients: an observational study. *Intensive Care Med* 32:1845–1850
- Lemaire F (2006) The European Directive 2001/20 for clinical research: Friend or foe? *Intensive Care Med* 32:1689–1690
- Harvey SE, Elbourne D, Ashcroft J, Jones CM, Rowan K (2006) Informed consent in clinical trials in critical care: experience from the PAC-Man Study. *Intensive Care Med* 32:2020–2025
- Lemaire F (2006) The inability to consent in critical care research: Emergency or impairment of cognitive function? *Intensive Care Med* 32:1930–1932
- Rego Lins Fumis R, Nishimoto IN, Deheinzeln D (2006) Measuring satisfaction in family members of critically ill cancer patients in Brazil. *Intensive Care Med* 32:124–128
- Benoit DD, Depuydt PO, Vandewoude KH, Offner FC, Boterberg T, De Cock CA, Noens LA, Janssens AM, Decruyenaere JM (2006) Outcome in severely ill patients with hematological malignancies who received intravenous chemotherapy in the intensive care unit. *Intensive Care Med* 32:93–99
- Azoulay E, Afessa B (2006) The intensive care support of patients with malignancy: do everything that can be done. *Intensive Care Med* 32:3–5
- Walsh TS, Lee RJ, Maciver CR, Garrloch M, Mackirdy F, Binning AR, Cole S, McClelland DB (2006) Anemia during and at discharge from intensive care: the impact of restrictive blood transfusion practice. *Intensive Care Med* 32:100–109
- Walsh TS, Saleh EE, Lee RJ, McClelland DB (2006) The prevalence and characteristics of anaemia at discharge home after intensive care. *Intensive Care Med* 32:1206–1213
- Griffiths J, Gager M, Alder N, Fawcett D, Waldmann C, Quinlan J (2006) A self-report-based study of the incidence and associations of sexual dysfunction in survivors of intensive care treatment. *Intensive Care Med* 32:445–451
- Scales DC, Tansey CM, Matte A, Herridge MS (2006) Difference in reported pre-morbid health-related quality of life between ARDS survivors and their substitute decision makers. *Intensive Care Med* 32:1826–1831
- Granja C, Azevedo LF (2006) When (quality of) life is at stake and intensive care is needed: How much can we trust our proxies? *Intensive Care Med* 32:1681–1682
- Collaboration C, Bion J-F, Barrett H (2006) Development of core competencies for an international training programme in intensive care medicine. *Intensive Care Med* 32:1371–1383
- Cerra F, Benitez M, Blackburn G, Irwin R, Jeejeebhoy K, Katz D, Pingleton S, Pomposelli J, Rombeau J, Shronts E, Wolfe R, Zaloga G (1997) Applied nutrition in ICU patients. A consensus statement of the American College of Chest Physicians. *Chest* 111:769–778
- Zauner A, Schneeweiss B, Kneidinger N, Lindner G, Zauner C (2006) Weight-adjusted resting energy expenditure is not constant in critically ill patients. *Intensive Care Med* 32:428–434
- Radrizzani D, Bertolini G, Facchini R, Simini B, Bruzzone P, Zanforlin G, Tognoni G, Iapichino G (2006) Early enteral immunonutrition vs. parenteral nutrition in critically ill patients without severe sepsis: a randomized clinical trial. *Intensive Care Med* 32:1191–1198

28. Bertolini G, Iapichino G, Radrizzani D, Facchini R, Simini B, Bruzzone P, Zanforlin G, Tognoni G (2003) Early enteral immunonutrition in patients with severe sepsis: results of an interim analysis of a randomized multicentre clinical trial. *Intensive Care Med* 29:834–840
29. Nguyen NQ, Chapman M, Fraser RJ, Ritz M, Bryant LK, Butler R, Davidson G, Zacharakis B, Holloway RH (2006) Long-standing type II diabetes mellitus is not a risk factor for slow gastric emptying in critically ill patients. *Intensive Care Med* 32:1365–1370
30. Lee AJ, Eve R, Bennett MJ (2006) Evaluation of a technique for blind placement of post-pyloric feeding tubes in intensive care: application in patients with gastric ileus. *Intensive Care Med* 32:553–556
31. van der Spoel JI, Schultz MJ, van der Voort PH, de Jonge E (2006) Influence of severity of illness, medication and selective decontamination on defecation. *Intensive Care Med* 32:875–880
32. Brienza N, Dalfino L, Cinnella G, Diele C, Bruno F, Fiore T (2006) Jaundice in critical illness: promoting factors of a concealed reality. *Intensive Care Med* 32:267–274
33. Provoost V, Cools F, Bilsen J, Ramet J, Deconinck P, Vander Stichele R, Vande Velde A, Van Herreweghe I, Mortier F, Vandenplas Y, Deliens L (2006) The use of drugs with a life-shortening effect in end-of-life care in neonates and infants. *Intensive Care Med* 32:133–139
34. Truog RD (2006) End-of-life care: Is euthanasia the answer? *Intensive Care Med* 32:6–8
35. Bush A (2006) Spinal muscular atrophy with respiratory disease (SMARD): an ethical dilemma. *Intensive Care Med* 32:1691–1693
36. Giannini A, Pinto AM, Rossetti G, Prandi E, Tiziano D, Brahe C, Nardocci N (2006) Respiratory failure in infants due to spinal muscular atrophy with respiratory distress type 1. *Intensive Care Med* 32:1851–1855
37. Heinrich S, Schiffmann H, Frerichs A, Klockgether-Radke A, Frerichs I (2006) Body and head position effects on regional lung ventilation in infants: an electrical impedance tomography study. *Intensive Care Med* 32:1392–1398
38. Wolf GK, Arnold JH (2006) Electrical impedance tomography: Ready for prime time? *Intensive Care Med* 32:1290–1292
39. Zaramella P, Freato F, Grazzina N, Saraceni E, Vianello A, Chiandetti L (2006) Does helmet CPAP reduce cerebral blood flow and volume by comparison with Infant Flow driver CPAP in preterm neonates? *Intensive Care Med* 32:1613–1619
40. Lindwall R, Svensson ME, Frostell CG, Eksborg S, Gustafsson LE (2006) Workplace NO and NO(2) during combined treatment of infants with nasal CPAP and NO. *Intensive Care Med* 32:2034–2041
41. Hummler HD, Engelmann A, Pohlant F, Franz AR (2006) Volume-controlled intermittent mandatory ventilation in preterm infants with hypoxic episodes. *Intensive Care Med* 32:577–584
42. Herber-Jonat S, Rieger-Fackeldey E, Hummler H, Schulze A (2006) Adaptive mechanical backup ventilation for preterm infants on respiratory assist modes: a pilot study. *Intensive Care Med* 32:302–308
43. Manna SS, Durward A, Moganasundram S, Tibby SM, Murdoch IA (2006) Retrospective evaluation of a paediatric intensivist-led flexible bronchoscopy service. *Intensive Care Med* 32:2026–2033
44. Boluyt N, Bollen CW, Bos AP, Kok JH, Offringa M (2006) Fluid resuscitation in neonatal and pediatric hypovolemic shock: a Dutch Pediatric Society evidence-based clinical practice guideline. *Intensive Care Med* 32:995–1003
45. Carcillo JA, Tasker RC (2006) Fluid resuscitation of hypovolemic shock: acute medicine's great triumph for children. *Intensive Care Med* 32:958–961
46. Lemmer J, Stiller B, Heise G, Hubler M, Alexi-Meskishvili V, Weng Y, Redlin M, Amann V, Ovroutski S, Berger F (2006) Postoperative phrenic nerve palsy: early clinical implications and management. *Intensive Care Med* 32:1227–1233
47. Dagan O, Nimri R, Katz Y, Birk E, Vidne B (2006) Bilateral diaphragm paralysis following cardiac surgery in children: 10-years' experience. *Intensive Care Med* 32:1222–1226
48. Ross-Russell RI (2006) C 3, 4 and 5, keep the diaphragm alive. *Intensive Care Med* 32:1109–1111
49. Celebi S, Koner O, Menda F, Balci H, Hatemi A, Korkut K, Esen F (2006) Procalcitonin kinetics in pediatric patients with systemic inflammatory response after open heart surgery. *Intensive Care Med* 32:881–887
50. Lopez-Herce J, Sanchez C, Carrillo A, Mencia S, Santiago MJ, Bustinza A, Vigil D (2006) Transpyloric enteral nutrition in the critically ill child with renal failure. *Intensive Care Med* 32:1599–1605
51. Katragkou A, Kotsiou M, Antachopoulos C, Benos A, Sofianou D, Tamiolaki M, Roilides E (2006) Acquisition of imipenem-resistant *Acinetobacter baumannii* in a pediatric intensive care unit: a case-control study. *Intensive Care Med* 32:1384–1391
52. Taylor D, Durward A, Tibby SM, Thorburn K, Holton F, Johnstone IC, Murdoch IA (2006) The influence of hyperchloraemia on acid base interpretation in diabetic ketoacidosis. *Intensive Care Med* 32:295–301
53. Morris KP, Forsyth RJ, Parslow RC, Tasker RC, Hawley CA, UK Paediatric Traumatic Brain Injury Study Group, Paediatric Intensive Care Society Study Group (2006) Intracranial pressure complicating severe traumatic brain injury in children: monitoring and management. *Intensive Care Med* 32:1606–1612
54. Goldstein B, Giroir B, Randolph A (2005) International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 6:2–8
55. Stephens RC, Fidler K, Wilson P, Barclay GR, Mythen MG, Dixon GL, Turner MW, Klein NJ, Peters MJ (2006) Endotoxin immunity and the development of the systemic inflammatory response syndrome in critically ill children. *Intensive Care Med* 32:286–294
56. Carcillo JA (2006) Searching for the etiology of systemic inflammatory response syndrome: Is SIRS occult endotoxemia? *Intensive Care Med* 32:181–184
57. Arkader R, Troster E-J, Lopes M-R, Junior R-R, Carcillo JA, Leone C (2006) Procalcitonin does discriminate between sepsis and systemic inflammatory response syndrome. *Arch Dis Child* 91:117–120
58. Khilnani P, Sarma D, Zimmerman J (2006) Epidemiology and peculiarities of pediatric multiple organ dysfunction syndrome in New Delhi, India. *Intensive Care Med* 32:1856–1862