Clinical review

Recent advances

Recent advances in intensive care

Stephen Stott

Grampian University Hospitals Trust, Aberdeen AB25 2ZN
Stephen Stott *consultant in anaesthesia and intensive care*
s.a.stott@abdn.ac.uk

BMJ 2000;320:358–61

Intensive care medicine has had its fair share of publicity over the past few years but mainly for reasons of shortness of resources rather than major medical advances. Despite this and the difficulty of doing research in this heterogeneous and relatively small population group, there have been several significant advances in the past few years. This article discusses some of these as well as the advances in training that have recently taken place.

Recent advances

- Mortality from the acute respiratory distress syndrome is decreasing as increased understanding of its pathophysiology leads to targeted treatments
- A trial by the US National Institutes of Health investigating a protective ventilatory strategy has been halted early in favour of reduced airway pressure ventilation
- Immunonutrition is a novel method of disease modification now being used in critically ill patients; recent work shows improvement in mortality using omega 3 polyunsaturated fatty acids
- Percutaneous tracheostomy is now accepted as a cost effective and improved method of airway management
- A recognised and structured career path in intensive care medicine has recently been established in the United Kingdom

Methods

I wrote this review using information from articles found through the Medline database on topics that I selected. Because of space restrictions it cannot be a comprehensive review of all recent advances. Key words used in the database search included nutrition, intensive care, acute respiratory distress syndrome, and tracheostomy

Acute respiratory distress syndrome

It is now over 30 years since the acute respiratory distress syndrome was described, and it is now known to be the extreme end of a continuum of lung injury. A consensus definition in 1994 (box)[1] has allowed accurate classification of lung injury and better standardisation in clinical research. The early reported mortality of 60% now seems to be falling, with recent reports of 30-40% from both the United States[2] and the United Kingdom,[3] but the reasons for this improvement are still unclear. As these patients usually do not die of respiratory failure but of the development of multiple organ failure, no single treatment that may attenuate the lung injury is likely to be responsible for the increased survival. The improvement in general care, attention to areas such as infection and nutrition, and a better understanding of the pathophysiology of the disease process have contributed substantially to the improved survival. Several areas, however, deserve mention.

Mechanical ventilation

Although ventilation is the mainstay of support for acute respiratory failure, it is now recognised that this can itself lead to damage in both normal and diseased lungs. The acute respiratory distress syndrome is not a homogenous disease, having areas of normal and diseased lung adjacent to each other. Diseased lung requires greater distending pressures and volumes to open and recruit involved alveoli. This can lead to pressure damage (barotrauma) or volume damage (volutrauma) in adjacent, normal, compliant lung units. This, and the shearing forces exerted because of repeated opening and closing of stiff alveoli, results in inflammation that can worsen and prolong the lung injury. Recognition of this ventilator induced lung injury has led to the investigation of so-called protective strategies of ventilation. These strategies lower distending pressures and volumes and split alveoli open with higher levels of positive end expiratory pressure. Differing results have been reported for such strategies: Amato and coworkers reported an increase in oxygenation and a decrease in 28 day mortality[4]; other workers have not repeated this result,[5] but a recent trial by the National Heart, Lung, and Blood Institute (US National Institutes of Health) into protective ventilator strategy has been stopped early after enrolment of 800 of the proposed 1000 patients because of a 25% reduction in mortality in those assigned to the smaller tidal volume group.[6]

Inhaled therapy

The pathophysiology of the acute respiratory distress syndrome includes pulmonary vasoconstriction, leading to ventilation and perfusion mismatching and systemic hypoxia. Administering vasodilating agents by the inhalational route can avoid systemic effects and can lead to improvements in arterial oxygenation as ventilated alveoli become better perfused. Attention has focused on agents that are rapidly inactivated, thus minimising systemic effects. Nitric oxide, a potent vasodilator, has now been well studied in the treatment of refractory hypoxia in acute lung injury. It is produced as medical grade gas in cylinders and is relatively easily delivered into the inspiratory limb of the breathing circuit. It does, however, need specialised monitoring equipment as products of its combination with oxygen include nitrogen dioxide. It is avidly bound to haemoglobin, and so its effects are short lasting and systemic hypotension is rare. It has been shown to improve oxygenation in so-called responders with acute lung injury but so far has not been shown to increase survival.[7 8] UK guidelines have been produced for its use.[9] Prostacyclin, another powerful pulmonary vasodilator, is easier to administer. Used with an infusion pump connected to a continuous nebuliser in the inspiratory limb of the circuit, it has also been shown to improve oxygenation.[10]

Prone position

Traditionally, patients are nursed supine in intensive care. Although it has been known since 1976 that an alteration in body position to prone will improve oxygenation in patients with the acute respiratory distress syndrome,[11] this measure has only recently been applied clinically. After Gattinoni and colleagues showed the effects that changing the body position have on ventilation distribution in these patients[12] numerous studies have now shown an improvement in oxygenation when patients are turned to prone position.[13 14] This can be achieved with minimal complications despite the presence of multiple indwelling vascular lines. The optimum time before the patient is turned again to supine is unresolved, with some advocating regular timed intervals and others leaving patients prone until oxygenation deteriorates. The exact mechanism resulting in the improvement in oxygenation is not yet understood, but caudal movement of the diaphragm, a more uniform gradient of pleural pressure, and recruitment of collapsed alveoli will all lead to a decrease in shunt fraction and all play a part.

The next logical step was to combine the prone position with pulmonary vasodilator treatment, and two recent studies have shown an additive effect of inhaled nitric oxide given in the prone position.[15 16] Thus several therapeutic interventions seem to improve the measured oxygenation in these patients. Whether they will lead to a further reduction in mortality is unknown.

Because of the increase in inflammatory mediators seen in acute lung injury many anti-inflammatory agents have been tried, but with little success. The administration of corticosteroids to patients in the fibroproliferative stage of the disease without evidence of infection, however, has recently been shown to reduce mortality.[17] The numbers in this study were small, but the results warrant further investigation to identify methods of determining the therapeutic window and to establish the dose and optimal length of steroid administration.

Definition of acute lung injury and the acute respiratory distress syndrome

Acute lung injury

- Oxygenation: arterial oxygen tension/fractional inspired oxygen < 300 mm Hg (despite normal arterial carbon dioxide tension and regardless of positive end expiratory pressure)*
- Chest radiography: bilateral diffuse infiltrates
- Cardiac: no apparent cardiogenic cause (pulmonary wedge pressure ≤ 18 mm Hg or 2.4 kPa if measured, or no clinical evidence of left atrial hypertension)

Risk factor: known triggering event or risk factor

Acute respiratory distress syndrome

As for acute lung injury except:

- Oxygenation: arterial oxygen tension/fractional inspired oxygen < 200 mm Hg (despite normal arterial carbon dioxide tension and regardless of positive end expiratory pressure)*

*The criterion for arterial oxygen tension/fractional inspired oxygen is arbitrary

Nutrition

The concept that altering diet can change outcome is not new in medicine and has now been applied to critically ill people. Accurate nutritional targets are important as both overfeeding and underfeeding have led to increased morbidity. Interest has now shifted to the ingredients of diet. Vitamins A, C, and E, as well as the amino acids arginine[18] and glutamine,[19] have all been shown to boost immune function, as have ribonucleotides and a change from omega 6 to omega 3 free fatty acids.[20] These fatty acids function as important regulators of numerous cellular functions and affect many cell signalling pathways. Membrane fluidity, ion channel flow, and cell surface receptor function (as well as the generation of prostaglandins, leukotrienes, cytokines, and expression of inflammatory gene products) are some of the processes involved. The switch

Chest radiograph showing radiological features consistent with acute respiratory distress syndrome

Fatty acids

Fatty acids function as second messengers and coregulators of gene transcription. Manipulation using diet has now been shown to reduce mortality and morbidity in intensive care patients

from omega 6 to omega 3 fatty acids is associated with a reduction in the production of proinflammatory mediators. Early studies comparing different formulations did not match energy or protein intake, but this shortcoming has now been addressed. Recent studies have concentrated on intensive care patients and shown a reduction in infective complications, days on a ventilator, and length of stay, but so far mortality has not improved.[21 22] The best formulation and which group of patients will benefit most have yet to be elucidated. In an attempt to do this, Gadek et al conducted a prospective randomised, double blind, multicentre study using eicosapentaenoic acid (an omega 3 polyunsaturated fatty acid) and γ linolenic acid (an omega 6 polyunsaturated fatty acid) plus antioxidants in patients with the acute respiratory distress syndrome. They showed faster resolution of lung inflammation, as assessed by inflammatory cells in bronchial-alveolar lavage fluid, and faster improvement in the ratio of fractional inspired oxygen to arterial oxygen tension in those receiving the study feed[23]; these patients also had shorter ventilator requirements, shorter stays in intensive care, and fewer new organ failures.

Patients unable to tolerate enteral feed can be fed parenterally. Glutamine, which in health is a non-essential amino acid, becomes severely depleted in critically ill patients but has not been added to total parenteral nutrition solutions because of stability problems. Griffiths and colleagues overcame this, showing that total parenteral nutrition supplemented with glutamine resulted in a reduction in mortality at six months.[24]

Equipment and monitoring

Evidence for the benefit of the plethora of equipment in intensive care units is sparse, but some equipment has become synonymous with these units. The pulmonary artery flotation catheter has been the bedrock of invasive cardiovascular monitoring since its introduction in 1976, but doubt has been raised about its value after a paper arising from the SUPPORT trial in the United States.[25 26] This showed an increase in 30 day mortality (odds ratio 1.24, confidence interval 1.03 to 1.49) associated with its use. A propensity scoring system was used to compare patients managed with and without a catheter. The furore that this has caused still reverberates in the world of intensive care, with some calling for a complete moratorium on its use.[27] The European Society of Intensive Care Medicine has since produced guidelines for its use,[28] and trials are under way to try to resolve this issue.[29] The important variable seems unlikely to be the catheter itself; it is more likely to be the indication for its use and the actions taken on the data produced by it.

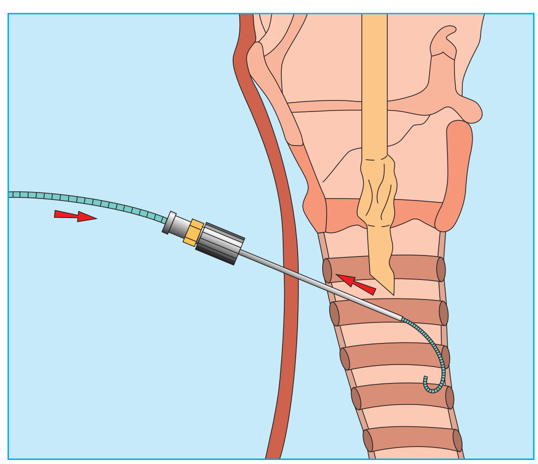
In the next few years non-invasive or low-invasive methods of assessing the cardiovascular system are likely to find their niche,[30 31] although they will have to show cost effectiveness in a field that already consumes a large slice of health resources. As extensive investigations into oxygen supply and demand relations have queried the relation between cardiac output and tissue oxygenation,[32] it remains to be seen if global cardiac output measurement and manipulation is the correct road to go down.

Tracheostomy

Tracheostomy is used frequently in critically ill patients—to facilitate weaning from mechanical ventilation, for patients' comfort, to ease tracheobronchial toilet, or for airway protection. Formal surgical tracheostomy requires transporting the patient to the operating theatre and the support of the theatre and anaesthetic team and is associated with a significant complication rate.[33] Bedside percutaneous dilatational tracheostomy was first described in 1985,[34] and several modifications have been reported since.[35] It has now become an established part of intensive care and is a cost effective procedure.[36] The trachea is located with a needle between the second and third rings and a guidewire inserted. Serial dilatation over the wire then allows the tracheostomy tube to be inserted. Chances of misplacement are reduced if bronchoscopic guidance is concurrently used,[37] and follow up series show that both early and late morbidity is lower than with open surgery.[38]

Intensive care training

In 1993 the Royal Colleges of Anaesthetists, Physicians, and Surgeons established the Intercollegiate Committee on Intensive Therapy to set up training programmes for trainees who wished either to be a consultant or to have a significant input in intensive care medicine. It put forward proposals on exposure for medical students and requirements for doctors already registered. Implementation of these recommendations has become the responsibility of the Intercollegiate Board for Training in Intensive Care Medicine. Trainees have to undertake at least 3 months' intensive care medicine as a senior house officer, ideally in a unit that is recognised by the board.



Location of the tracheal lumen with guidewire for percutaneous tracheostomy

They then undergo intermediate training in intensive care medicine, consisting of six months in intensive care and six months in a complementary specialty—for example, anaesthesia for a physician or acute general medicine for an anaesthetist. Surgeons need exposure to both anaesthesia and medicine.

For those who will have a near full time commitment to intensive care medicine or be unit directors there needs to be a further year's training (advanced training) to cover the organisational aspects of intensive care and exposure to specialised units. The board has submitted an application for specialty status to the Specialist Training Authority for recognition as a schedule 2 specialty. A diploma in intensive care medicine had its first sitting in July 1998. Over 100 units have now been granted interim recognition for training, and a body of advisers in intensive care medicine has been appointed, including regional advisers, to ensure continuing passage of information and maintenance of standards. Further details regarding training can be downloaded from the board's web page (www.ncl.ac.uk/nsa/ibtic).

Funding: None.
Competing interests: None declared.

1 Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial co-ordination. *Am J Respir Clin Care Med* 1994;194:818-24.
2 Milberg JA, Davis DR, Steinberg KP, Hudson LD. Improved survival of patients respiratory distress syndrome (ARDS): 1983-1993. *JAMA* 1995;273:306-9.
3 Abel SJC, Finney SJ, Brett SJ, Keogh BF, Morgan CJ, Evans TW. Reduced mortality in association with the acute respiratory distress syndrome (ARDS). *Thorax* 1998;53:292-4.
4 Amato MBP, Barbas CSV, Medeiros DM, Magaldi RB, Schettino GP. Effect of a protective-ventilation strategy on mortality in acute respiratory distress syndrome. *N Engl J Med* 1998;338:347-54.
5 Stewart TE, Meade MO, Cook DJ, Granton JT, Hodder RV, Lapinsky SE, et al. Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk of developing the acute respiratory distress syndrome. *N Engl J Med* 1998;338:355-61.
6 www.hedwig.mgh.harvard.edu/ardsnet (accessed 14 December 1999).
7 Dellinger RP, Zimmerman JL, Taylor RW, Straube RC, Hauser DL, Criner GJ, et al. Effects of inhaled nitric oxide inpatients with acute respiratory distress syndrome: results of a randomised phase II trial. *Crit Care Med* 1998;26:15-24.
8 Lundin S, Mang H, Smitheies M, Stenqvist O, Frostell C. Inhalation of nitric oxide in acute lung injury: results of a European multicentre study. *Intensive Care Med* 1999;25:911-9.
9 Cuthbertson BH, Dellinger P, Dyar OJ, Evans TE, Higenbottam T, Latimer R, et al. The UK guidelines for the use of inhaled nitric oxide therapy in adult ICU's. *Intensive Care Med* 1997;23:1212-8.
10 Zwissler B, Kemming G, Habler O, Kleen M, Merkel M, Haller M, et al. Inhaled prostacyclin (PGI2) versus inhaled nitric oxide in adult respiratory distress syndrome. *Am J Respir Crit Care Med* 1996;154: 1671-7.
11 Piehl MA, Brown RS. Use of extreme position change in acute respiratory failure. *Crit Care Med* 1976;4:13-4.
12 Gattinoni L, Pelosi P, Vitale G, Presenti A, D'Andrea L, Macheroni D. Body changes redistribute lung computed tomographic density in patients with acute respiratory failure. *Anaesthesiology* 1991;74:15-23.
13 Jolliet P, Bulpa P, Chevrolet JC. Effects of prone position on gas exchange and hemodynamics in severe acute respiratory distress syndrome. *Crit Care Med* 1998;12:1977-85.
14 Flaaten H, Aardel S, Hevroy O. Improved oxygenation using the prone position in patients with ARDS. *Acta Anaesthiol Scand* 1998;3:329-34.
15 Papazian L, Bregeon F, Gaillet F, Thirion X, Gainnier M, Gregoire R, et al. Respective and combined effects of prone position and inhaled nitric oxide in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 1998; 157:580-5.
16 Germann P, Ziesche R, Leitner C, Roeder G, Urak G, Zimpfer M, et al. Additive effects of nitric oxide inhalation on the oxygenation benefit of the prone position in the acute respiratory distress syndrome. *Anaesthesiology* 1998;89:1401-6.
17 Meduri GU, Headley AS, Golden E, Carson SJ, Umberger RA, Kelso T, et al. Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 1998;280:159-65.
18 Brittenden J, Watmough D, Eremin O. L-arginine stimulates host defences in patients with breast cancer. *Surgery* 1994;115:205-12.
19 O'Riordain MG, Fearon KC, Ross JA, Rogers P, Falconer JS, Bartolo DC, et al. Glutamine-supplemented total parenteral nutrition enhances T-lymphocyte response in surgical patients undergoing colorectal resection. *Ann Surg* 1994;220:212-21.
20 Blok WL, Katn MB, ven der Meer JW. Modulation of inflammation and cytokine production by dietary (n = 3) fatty acids. *J Nutr* 1996;126;1515-33.
21 Atkinson S, Sieffert E, Bihari D. A prospective, randomized, double-blind, controlled clinical trial of enteral immunonutrition in the critically ill. Guy's Hospital Intensive Care Group. *Crit Care Med* 1998;26:1164-72.
22 Beale RJ, Bryg DJ, Bihari DJ. Immunonutrition in the critically ill: a systemic review on clinical outcome. *Crit Care Med* (in press).
23 Gadek JE, DeMichele SJ, Karstad MD, Pacht ER, Donahoe M, Albertson TE, et al. Effect of enteral feeding with eicosapentaenoic acid, (γ linolenic acid and antioxidants in patients with acute respiratory distress syndrome. *Crit Care Med* 1999;27:1409-20.
24 Griffiths RD, Jones C, Palmer TE. Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition. *Nutrition* 1997;13:295-302.
25 SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill patients. The study to understand prognosis and preferences for outcomes and risks of treatment (SUPPORT). *JAMA* 1995;274:1591-8.
26 Connors AF Jr, Speroff T, Dawson NV, Thomas C, Harrell FE Jr, Wagner D, et al. The effectiveness of right heart catheterisation in the initial care of critically ill patients. *JAMA* 1996;276:889-97.
27 Dalen JE, Bone RC. Is it time to pull the pulmonary catheter? *JAMA* 1996;276:916-8.
28 European Society of Intensive Care Medicine Expert panel. The use of the pulmonary artery catheter. *Intensive Care Med* 1991;17:I-VIII.
29 Sandham JD, Hull RD, Brant RF. The pulmonary artery takes a great fall. *Crit Care Med* 1998;26:1288-9.
30 Cariou A, Monchi M, Joly LM, Bellenfant F, Claessens YE, Thebert D, et al. Non-invasive cardiac output monitoring by aortic blood flow determination: evaluation of the Sometec Dynemo-3000 system. *Crit Care Med* 1998;26:2066-72.
31 Poelaert J, Schmidt C, Van Aken H, Hinder F, Mollhoff T, Loick HM. A comparison of transoesophageal echocardiographic Doppler across the aortic valve and the thermodilution technique for estimating the cardiac output. *Anaesthesia* 1999;54:128-36.
32 Pinsky MR. Beyond global oxygen supply-demand relations: in search of measures of dysoxia. *Intensive Care Med* 1994;20:1-3.
33 Heffner JE, Miller KS, Sahn SA. Tracheostomy in the intensive care unit. II. Complications. *Chest* 1986;14:742.
34 Ciaglia P, Firsching R, Syniec C. Elective percutaneous dilatational tracheostomy: a new simple bedside procedure—preliminary report. *Chest* 1985;87:715.
35 Schachner A, Ovil Y, Sidi J, Rogev M, Heilbronn Y, Levy MJ. Percutaneous tracheostomy—a new method. *Crit Care Med* 1989;17:1052-6.
36 Cobean R, Beals M, Moss C, Bredenberg CE. Percutaneous dilatational tracheostomy. A safe, cost-effective bedside procedure. *Arch Surg* 1996;131:265-9.
37 Winkler W-B, Karnik R, Seelman O, Havlicek J, Slany J. Bedside percutaneous dilatational tracheostomy with endoscopic guidance: experience with 71 ICU patients. *Intensive Care Med* 1994;20:476-9.
38 Hill BB, Zweng TN, Maley RH, Charash WE, Toursarkissian B, Kearney P. Percutaneous dilatational tracheostomy: report of 356 cases. *J Trauma* 1996;41:238-43.

Corrections and clarifications

Increase in congenital rubella occurrence after immunisation in Greece: retrospective survey and systematic review
In this paper by Takis Panagiotopoulos and colleagues (4 December 1999, pp 1462-7), the first sentence of the final paragraph of the results section (p 1465) should have read: "Only sporadic cases of congenital rubella were reported in Greece in 1950-92: 1952 (one case), 1954-5 (five), 1974-85[13] [[not 1974-85[13]]], 1980 (one), 1983 (three), and 1986-7 (four).[w43w49]

Obituaries
In the obituary of Dr Alan James Mathams (1 January, p 61) his date of birth should have been given as 1953, not 1933.

The price of coffins: specious arguments by eminent doctors against the dangers of tobacco
In this article by P Cowen (18-25 December, pp 1621-3) the word "cigarette" was wrongly omitted from the first sentence of the second paragraph. The sentence should have ended: "I have not smoked a cigarette since."

Hypericum extract versus imipramine or placebo in patients with moderate depression: randomised multicentre study of treatment for eight weeks
In this paper by Philipp and colleagues (11 December, pp 1534-8) a "t" was missing from the corresponding author's email address; the correct address is kohiller.steiner@t-online.de [not kohiller.steiner@-online.de].