The Changing Pattern of Post-traumatic Respiratory Distress Syndrome

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During a one year period, 78 patients at the Denver General Hospital required mechanical ventilation following injury. Thirteen patients were judged to have Respiratory Distress Syndrome. Of these, 9 had classic early onset RDS but, with intravenous fluid restriction following resuscitation, diuretics and careful mechanical ventilation, all recovered. Six patients, all of whom were septic, developed late onset RDS 5 or more days after injury; 5 died. Disparity between early and late onset RDS is emphasized; the one with good, the other with dismal prognosis. The current need is to improve treatment of late onset RDS, which frequently is associated with bacterial infection.

POST-TRAUMATIC respiratory distress syndrome (RDS) came into explosive prominence during management of combat casualties in the Vietnam War.[13,18,22,25-27] Since then an enormous volume of literature has evolved concerning its pathogenesis, recognition and care.[4,6,8] Main emphasis has remained, as during the War, on development of respiratory failure in the immediate post-injury period associating the syndrome with chest wall contusion,[22] blast,[21] multiple blood transfusions,[10,19] fat embolism,[2,12] aspiration,[5] shock,[9] cerebral hypoxia, and fluid and sodium overload.[26] In a series of classic articles, Ashbaugh[1,3,18,23] described the adult respiratory syndrome and later reviewed experience with 31 patients who died of the lesion, 19 of whom had pulmonary sepsis. He emphasized that infection complicated prolonged ventilation.

As part of our interest in developing a membrane oxygenator to provide prolonged ventilatory support in RDS we reviewed the pattern of post-trauma RDS over a one-year period. Our aim was to define indications for this technique which is now technically feasible.[7,15-17]

In this paper we show that pulmonary insufficiency in the immediate post-injury period if treated vigorously is not usually fatal. Instead, RDS of late onset associated with generalized or pulmonary sepsis is the important life-threatening lesion toward which prolonged oxygenator support will have to be directed.

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Clinical Experience

During the period of January 1, 1973 to January 1, 1974, 78 patients at the Denver General Hospital were administered endotracheal mechanical ventilation following injury. This amounted to approximately 14% of all patients operated upon for major trauma during this period. Situated in the center of the city and served by efficient police-dispatched ambulances, we received many severely wounded who would have expired under less ideal emergency care systems.

Denver is 5,280 feet above sea level. Arterial pO_2 is 74mmHg in a normal person breathing room air. There is, therefore, a slight but appreciable decrease in ventilatory reserve that may make the patient more prone to RDS at this altitude than at sea level.

The mean age of these 78 injured patients requiring ventilatory support was 39 years, with a range of 16-81 years. Sixty-nine patients were males and 9 were females.

Hospital death rate was 44% (34/78), but only 5 (6%) of these patients died primarily of pulmonary insufficiency. Table 1 shows the cause of death. The 5 pulmonary deaths represent 15% of the total deaths. Twenty-two (64%) were due to brain injury; two (6%) to hepatorenal failure; three (9%) to septic shock, one (3%) to cardiac failure, and another to exsanguination (3%). As emphasized by Moore,[26] the greatest killer is late secondary organ (heart, lung, liver and kidney) failure.

TABLE 1. *Cause of Deaths: 34 Patients (44% of Patients Ventilated)*

	# Patients	%
Brain Injury	22	64%
Pulmonary Insufficiency	5	15%
Septic Shock	3	9%
Hepato-renal Failure	2	6%
Cardiac Failure	1	3%
Exanguination	1	3%
Total	34	100%

Types of Injury in Patients Requiring Mechanical Ventilation

Head Injury. Brain swelling, the characteristic final common pathway to death following head injury, is potentiated by hypoxia and hypercarbia. We believe assisted mechanical ventilation is accepted neurosurgical treatment in such patients.[28] Of the 78 total patients, 31 (39%) suffered head injury, often in association with other trauma. Twenty patients had closed head injury and 11 had open injuries. The mortality in these severe head injury patients was 71%, but only two (6%) of these deaths were due to respiratory failure. Neither of the dying patients had ventilatory problems in the immediate post-injury period. Both suffered closed head trauma and both apparently were recovering from their brain injury with recession of unconsciousness when pulmonary sepsis intervened and they died of pulmonary insufficiency 19 and 21 days following injury.

Thoracic Injury. During this 12-month period we cared for 140 patients with major thoracic trauma. Sixteen patients required thoracotomy (14%); 10 for pericardial tamponade or actively bleeding cardiac wounds; 5 for massive intrathoracic bleeding; and one as a part of other resuscitative efforts. All 16 patients required postoperative ventilation, but only 3 thoracotomy patients developed significant RDS. There were no deaths ascribable to the RDS.

TABLE 2. *Early Onset RDS: 9 Patients (11.5% of patients ventilated)*

Injury	Day Onset RDS	Duration	Etiology
1. Extremity fracture	2	3	Fat embolus
2. Avulsion arm	2	4	Shock
3. Blunt chest trauma	1	3	Pulmonary contusion
4. Blunt chest trauma	1	2	Pulmonary contusion
5. Blunt chest trauma	1	2	Pulmonary contusion
6. Flail chest	1	4	Pulmonary contusion
7. Flail chest*	1	5	Pulmonary contusion
8. GSW heart	1	4	Shock
9. Stab (lung, liver, internal mammary artery)**	1	5	Shock

*Recovered from initial RDS—sepsis, pneumonia 2-3 weeks later; died with late onset RDS.

**Early onset RDS resolved—then pneumonia—lived after 30 days on ventilator.

Six patients were mechanically respired for a mean of 14 days for flail chest. Two flail chest patients had florid RDS secondary to pulmonary contusion. One was ventilated 14 days but by the day 4 post-injury his RDS had cleared and ventilatory support was maintained until his chest wall stabilized and he recovered. The other patient with a flail chest similarly recovered from his early RDS but after 2 weeks, while still on the respirator, developed complicating sepsis and died on 43 days post-injury.

Six other patients had pulmonary contusion secondary to blunt trauma, and 3 developed RDS immediately after injury. They were mechanically ventilated a mean of only 2 days. Characteristically their acute symptoms and alarming roentgenologic findings cleared promptly under our current regime of adequate ventilation, fluid restriction and diuretics after the initial period of resuscitation.

Abdominal Injury. None of the 14 patients requiring mechanical ventilation following major vascular or abdominal injury developed RDS. A number of these injured patients bled from stress ulcer associated with intraabdominal sepsis,[29] but in them the stomach, not the lung, was the secondary target organ.

Extremity and Spine Injuries. Despite the large number of extremity injuries cared for by our Orthopedic Division (350 annually), only two patients, solely with extremity injuries, developed RDS sufficiently severe to require mechanical ventilation. One patient had classic fat embolism, requiring mechanical ventilation for 4 days.

Another patient with a fractured hip and chronic lung disease developed late (day 6 post-injury) respiratory insufficiency and died on day 19 post-injury of Klebsiella pneumonia. Postmortem showed evidence of multiple focal pulmonary emboli but the predominant process was bronchopneumonia.

Burns. Two patients with extensive burns were ventilated. Neither had inhalation burns. One died on the 21st post-burn day of liver and kidney failure. The other died on the 40th post-burn day in bacteremic hypotension and had severe RDS.

Early vs. Late Onset RDS

Two distinct patterns of RDS are discernible in this experience. They are so disparate as to represent two separate diseases or syndromes.

Early Onset RDS becomes manifest within hours after injury. Its course, though clearly life-threatening by reason of severely impaired blood oxygenation, is self-limited.

As shown in Table 2, 9 patients developed respiratory insufficiency within 12 hours after injury and were categorized as suffering early onset RDS. Causes of injury were (1) blunt chest trauma (5); (1) GSW or stab of chest (2); avulsion of arm and exsanguination, and fat

TABLE 3. *Late Onset RDS: 5 Patients (6.4% of patients ventilated)*

Injury	Day Onset RDS	Duration	Etiology
1. Flail chest	14	29	Sepsis
2. Fractured hip	5	13	COPD & pneumonia
3. Burn (50%)	23	17	Aspiration pneumonia
4. Blunt head injury	9	10	Pneumonia
5. Blunt head injury	5	12	Pneumonia

embolism. Although all of these patients demonstrated the classic clinical, roentgenologic and blood gas abnormalities associated with RDS,[23] all recovered from their initial respiratory distress. One patient exsanguinated and had a cardiac arrest from avulsion of his arm by a conveyor belt prior to Emergency Department admission. He was resuscitated but was judged neurologically dead 4 days later. At autopsy his lungs were edematous, although this was not the cause of his death.

A second patient, stabbed in the internal mammary artery, lung and liver, was recovering from early onset RDS when on the 8th post-injury day she developed pneumonia and her RDS worsened. She required a total of 30 days of mechanical ventilation and after a long and complicated course she recovered. She thus showed manifestation of both early and late onset RDS.

Late Onset RDS. Six patients developed respiratory insufficiency 5 or more days after injury. One patient had experienced early onset respiratory distress prior to that time. As detailed in Table 3, each had significant pulmonary sepsis associated with the respiratory distress and 5 of the 6 died. Late onset, sepsis and death were the apocalyptic triad. The inexorable clinical course was progressive respiratory insufficiency, requiring increasing concentrations of F_IO_2 and pressures to ventilate the non-compliant lung before the patient died of pulmonary insufficiency or bacteremic hypotension.

Case Reports

Case 1. A 71-year-old man with known severe coronary disease sustained a flail chest and questioned myocardial contusion in an automobile accident. His pulmonary insufficiency was controlled early in the immediate post-injury period with a volume respirator and judicious use of intravenous fluids and diuretics. Two weeks following injury, while still on the respirator awaiting final stabilization of his chest wall, he asked to be and was transferred to another hospital. He developed gradual renal failure, bilateral pneumonia, generalized sepsis, and then underwent cholecystectomy. He died in respiratory failure and generalized sepsis 43 days after injury.

Case II. A 64-year-old housewife with known chronic obstructive disease fell and fractured her femur. Five days later she developed Klebsiella pneumonia, which was controlled with Keflin and Kanomycin. There was no clinical evidence of thrombophlebitis or pulmonary embolism. She died a septic and pulmonary death on the 18th post-injury day after onset of her respiratory syndrome.

Case III. A 40-year-old man suffered 50% third-degree burns. Despite partial skin graft coverage, he became septic and on the 23rd post-burn day vomited and aspirated stomach contents. He developed progressive bilateral pneumonia and required mechanical ventilation with increasing concentrations of oxygen. He died of respiratory insufficiency and sepsis 17 days after aspiration and 40 days after being burned.

Case IV. A 52-year-old alcoholic man suffered a closed head injury in a fall. On the 5th post-injury day his sputum grew Klebsiella and *D. pneumonia* and he was treated with chloramphenical. On day 9 post-injury he underwent craniotomy for intercerebral bleeding with good neurological result. Despite vigorous pulmonary hygiene and further antibiotic therapy with colistin and gentamycin, progressive pulmonary insufficiency caused his death 10 days postoperative. Mechanical ventilation with 100% F_IO_2 and positive end expiratory pressure of 5-10mm H_2O were to no avail.

Case V. A 43-year-old alcoholic man underwent surgery immediately following emergency admission for subdural and epidural hematomas caused by blunt head trauma. On day 5 postoperative his sputum grew *D. pneumonia* and penicillin therapy was begun. With progression of disease oxicillin and gentomycin were added. Response was poor and progressive respiratory insufficiency made mechanical respiration with 100% F_IO_2 mandatory. Despite vigorous treatment, he died 17 days postoperative of respiratory failure.

Discussion

The pattern of post-injury RDS has changed since it demanded such intense interest a few years ago during the Vietnam War. Respiratory insufficiency occurring immediately following injury still exists, but compulsive attention to fluid therapy, diuretics and adequate mechanical ventilation has aborted many attacks and has removed the life-threatening sting from many others. None of our patients in this busy trauma center died from early onset RDS during this 12-month period.

Our routine for management of patients at risk for post-injury RDS is not unique, save for meticulous attention to respiratory care in the few days immediately following injury. Three large caliber intravenous catheters are inserted while the patient is in the Emergency Department and Ringer's Lactate is given as required to

maintain satisfactory peripheral perfusion for the 15-30 minutes before cross-matched ACD blood becomes available. Whenever possible a millipore filter is used and changed with every 3rd unit. CVP is monitored via a subclavian or jugular vein. As soon as hemostasis is achieved, fluid and blood infusion is sharply limited and 20mg Furosamide (Lasix) is given and repeated as required. We do not wait for signs of RDS to develop, preferring the easier path of aborting the attack by fluid restriction. When there is major suspicion of pulmonary contusion, salt-poor albumin is occasionally used for resuscitation along with blood. Mechanical ventilation is initiated early via a cuffed endotracheal tube with early disregard for potential oxygen toxicity. Within a few hours F_IO_2 can be decreased to levels that will support arterial pO_2 of 70-100 mmHg. In the early post-injury hours, pulmonary capillary hypoxia is more threatening for subsequent RDS than is oxygen toxicity. Positive end expiratory pressure (PEEP) is used when the RDS is severe.

None of these principles or techniques is original but in the aggregate have, as the current experience typifies, minimized the threat of early onset post-injury RDS. None of our clinical series died of post-injury RDS.

Late onset RDS is in complete contrast in timing, etiology, resistance to mechanical ventilation and prognosis. We described 5 deaths: none had severe ventilatory problems in the immediate post-injury period. Common to them was sepsis, which could have been primary or a complication to other pulmonary problems. Identifiable factors in etiology are aspiration, bacterial pneumonia secondary to prolonged mechanical ventilation, pulmonary embolism (unproven in this series) and the pulmonary effects of generalized bacteremia. Multiple organ failure including the heart, kidneys and liver influences the lungs.

The precise mechanism by which bacteremia depresses pulmonary function is not known. Endotoxin, with its release of vasoactive amines causes increased pulmonary capillary permeability, which may play a part.[11] So too may the multiple microemboli associated with *E. coli* bacteremia.[14] Sepsis decreases synthesis of surfactant[24] which also may be of importance. Whatever the explanation, both generalized and pulmonic infection are associated with late onset RDS; and antibiotics are relatively ineffective in reversing the lesion.

Ashbaugh and Petty,[3] in a classic study of 51 patients with RDS, found sepsis in 36, of whom 25 died. Although their patients were not all post-injury, they emphasized the threat of infection during prolonged ventilatory assistance. Our current study with the injured confirms their thesis and, in addition, emphasizes the need to define why patients develop RDS with sepsis in the late post-injury period.

The original purpose of this study was to delineate the indications for prolonged membrane oxygenator support for post-injury RDS. They obviously are few. An occasional patient will probably benefit from prolonged membrane oxygenator support in the first few days following injury. For the most part this will be limited to the aged and to those with severe underlying lung disease.

The majority of candidates for oxygenator support will be those with late onset RDS associated with systemic or pulmonary sepsis. In patients who are otherwise salvageable and who do not have irreversible pulmonary fibrotic changes, prolonged oxygenation must be evaluated.

Intensive study of the cause, early diagnosis and prevention of early onset post-injury RDS has resulted in decreased incidence and improved salvage. It is now time to focus attention on the late onset analogue which still carries a fearful mortality.

Conclusions

A one year experience with 78 post-injury patients who required mechanical ventilatory support has been reviewed. Of the 13 patients judged to have RDS, 9 had classic early onset, but with fluid restriction following resuscitation, diuretics and careful mechanical ventilation, none died of early onset RDS. Five of the 6 patients who had late onset RDS died. All were septic. Disparity between the two types of RDS must be recognized. Late onset RDS provides the potential patient source for prolonged membrane oxygenator assistance.

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Discussion

Dr. Hiram C. Polk, Jr. (Louisville, Kentucky): I rise to strongly reemphasize everything that Dr. Eiseman has said. I think he's right on target about the pathogenesis of this illness, despite all of our misunderstood discussions of the last couple of years. His thesis is precisely consistent with the one that was developed by Bob Fulton and Cal Jones and presented from our Department at the College about six weeks ago and will be published in *SG&O* in February.

I would like to show some slides that underline each of these points rather clearly. (Slide) In a slightly larger series of patients treated in a slightly briefer period of time, we showed that there is a variable frequency of posttraumatic respiratory insufficiency associated with a variety of illnesses that we had earlier thought had been absolutely necessary for the ultimate development of such abnormalities.

(Slide) If you look at this large group of patients to clean out the "pure" group comparisons of etiologic factors, you find a number of things: that sepsis is infinitely more significant than multiple system injury; secondly, that massive fluid therapy is of small significance compared to sepsis; and that oligemic shock itself is very slightly significant compared to the development of sepsis of some sort or another.

You see not only by the P values, but the calculation of the power of the test, that this is extremely likely to be an accurate observation. Once more, these represent civilian victims of trauma, just as Dr. Eiseman has described.

The ultimate question to be asked, though, is: Which is the chicken, and which is the egg? Does the sepsis precede the respiratory failure, or is the respiratory failure a consequence of initial respiratory support with superimposed infection on a foreign body?

(Slide) Just as Dr. Eiseman has developed a very cogent discussion of the differential onset of the illness, I think you can see here that almost all of our patients developed posttraumatic respiratory insufficiency due to sepsis in the circumstance in which the sepsis preceded respiratory support. As a matter of fact, very infrequently did the causative events occur in the reverse relationship.

The point that Dr. Eiseman has raised is very clear, and another point, by inference, that he made is that the supportive care of an individual who is ill of respiratory distress syndrome due to sepsis with continued respiratory support is actually very unprofitable. The only chance that these individuals stand to recover from their illness is correction of the underlying sepsis.

Dr. Ben Eiseman (Closing discussion): I appreciate Dr. Polk's remarks. A few weeks ago, while Visiting Professor at Louisville, Dr. Jones and I found, by chance, the similarity of our findings and conclusions.

In our own experience, most of the sepsis proceeded late, but not early, post injury RDS. Why bacterial infection has such action on the lung I don't know, but we are currently exploring the mechanisms. Very likely they are those that similarly injure the liver causing liver failure or stomach stress ulcer.

Whatever the cause, the clinical corollary is obvious. Patients with pus as the possible cause of RDS (or hepatic coma or stress ulcer) are often too sick *not* to operate on. It may be the only chance to cure the RDS or other organ failure due to generalized bacteremia.

Ubi pus ibi evacua still pertains.