Acute Respiratory Distress Syndrome (ARDS)
University of Washington, Seattle, U.S.A.
Leonard D. Hudson, M.D.

This presentation will review new developments and research findings in acute lung injury (ALI) and ARDS, emphasizing (but not limited to) studies from the Seattle Specialized Center of Research (SCOR) on ARDS. The epidemiology, pathophysiology, and management of ARDS will be reviewed.

The definition of ARDS, from the first description in 1967 to the definition of ALI and ARDS by the 1994 American-European Consensus Conference on ARDS will be reviewed. This Conference tried to distinguish between milder forms of lung injury, called ALI, and ARDS by oxygenation (PaO$_2$/FIO$_2$) criteria but the usefulness of this distinction has been limited.

The risk factors and associated incidence of ARDS will be reviewed. The risk factors with the highest incidence that also occur commonly are sepsis syndrome (severe sepsis), severe trauma, and aspiration of gastric contents. Multiple emergency transfusion (>15 units of blood products in a 24 hour period) is a useful marker of severe trauma but is also associated with a high (35%) incidence of ARDS in patients with medical conditions.

Half of the patients who eventually develop ARDS will do so within 24 hours of risk onset and 80-90% within 72 hours. When patients first meet criteria for severe sepsis, many will already meet criteria for ALI or ARDS.

The mechanisms of lung injury in ARDS can either be direct (e.g. aspiration of gastric contents) or, more commonly, indirect (e.g., sepsis or severe trauma). Indirect mechanisms are thought to be related to intravascular activation of inflammation with pro-inflammatory cytokines and other mediators being present in excess of anti-inflammatory inhibitors or blockers. Some evidence suggests that sustained alveolar inflammation is associated with worse outcome. Marked fibrosis of the lung is known to be a common pathologic finding in ARDS. Evidence suggests that increased fibrotic activity is also associated with worse outcome.

The management of ARDS is primarily supportive, including use of mechanical ventilation and positive end-expiratory pressure. Knowledge in this area is evolving and the optimal method of mechanical ventilation support is not clear. Recent animal model studies suggest that acute lung injury can be caused or propagated by some effects of mechanical ventilation; mechanisms of injury are speculated to include overdistention of lung units and cyclic reopening of collapsed alveoli. Controlled human studies are limited and only available in abstract form at this time. To date, the findings indicate no mortality benefit from low stretch (low tidal volume) ventilation compared to traditional or high stretch (high tidal volume) ventilation. A single center study of PEEP above the lower inflection point of the patient's pressure-volume curve (designed to prevent cyclic reopening) combined with low stretch ventilation has demonstrated a lower mortality compared to traditional methods of mechanical ventilation. This study requires confirmation. A practical approach to ventilatory management awaiting more definitive multi-center studies will be discussed.

To date, no pharmacologic anti-inflammatory therapy has been shown to be beneficial in a controlled clinical trial of patients with ARDS. One study of an artificial surfactant has shown promising but not conclusive results. Use of inhaled nitrous oxide (NO) and intravenous almitrine result in improved oxygenation in many patients but studies investigating effects of these drugs on outcome have not been completed. The late, sustained use of corticosteroids have suggested promise in uncontrolled series and a controlled trial is currently being conducted.

Improved mortality in patients with ARDS is suggested by review of ARDS registry data from Seattle (Harborview Medical Center) using the same definition of ARDS since 1982 and adjusting or accounting for differences in age, risk factor, and severity of illness. Further analysis suggests little difference in mortality in the first three days following ARDS onset (usually related to deaths from the underlying condition) but substantial mortality improvement after that time, suggesting that improved mortality may be a result of either fewer complications or decreased mortality associated with complications.