THE LUNG IN SHOCK: A REVIEW

JUDITH DOWD, M.D. AND
LEONARD C. JENKINS, B.A., M.D., C.M., F.R.C.P.(C)

I. INTRODUCTION

SUCCESS IN MANAGEMENT of haemodynamic and renal problems of shock has resulted in increasing emphasis on the importance of the respiratory failure component in shock.[1,2] The frequency of pulmonary problems increases with the severity of shock, especially if there is concurrent sepsis and/or previous cardiopulmonary disease.[3]

It is significant to note[4] that among severely injured patients one-third of deaths are due to direct involvement of a major organ (brain, heart, kidney) by the primary process, one-third are due to sepsis, usually from Gram negative organisms and one-third are due to progressive pulmonary failure. Since some of the cases in the first two instances also have respiratory complications at the time of death, it appears that 30 per cent to 50 per cent of patients who die following trauma and shock, have important pulmonary disease.[3,4]

During World War I severely traumatized patients usually did not survive long enough for a specific respiratory insufficiency syndrome to develop and to be recognized. Some patients who were initially resuscitated following severe shock, developed severe respiratory distress and the condition was termed "post-traumatic pulmonary massive collapse".[3] In World War II and during the Korean War, the term "wet lung" was used to refer to the pulmonary complications of thoracic and non-thoracic trauma.[5] However, the Vietnam War has brought this problem into prominence. With greatly improved means of evacuation of the severely injured to prompt medical attention, physicians have been impressed with the large numbers of patients who go on to develop respiratory complications, which are often fatal. These cases have prompted extensive clinical and laboratory research into the aetiology and pathogenesis of this condition. The term *"shock lung"* has been coined to refer to the syndrome of respiratory insufficiency developing after severe trauma and/or shock. Since not all patients who develop this syndrome have actually been in shock, however, this term may be inappropriate.

II. CLINICAL FEATURES

The syndrome has been divided into four clear cut phases:[4]

Phase I: This is the period of the shock state or injury and resuscitation. The patient has metabolic and respiratory alkalosis following the first few hours of low flow. Persistent spontaneous hyperventilation and hypocapnia, despite clear

From the Department of Anaesthesia, Vancouver General Hospital and Department of Anaesthesia, Faculty of Medicine, University of British Columbia.

lungs, may be the first indication that respiratory difficulties are pending. There is also an early mild lacticacidaemia.

Phase II: This is the period of stabilization and early respiratory distress. The clinical picture is improved, but hyperventilation persists, with resultant hypocapnia.[6] The patient also shows increasing venous admixture. The physiological shunt across the lungs may be 10 per cent to 20 per cent of the cardiac output. The patient can recover from this phase.

Phase III: The signs of respiratory difficulty become more marked. Intensive respiratory management is required, often including intermittent positive pressure ventilation. Hypocarbia persists if attempts are not made to control it. The alveolar-arterial oxygen gradient ($A–a\triangle O_2$) increases markedly and lacticacidaemia recurs, or becomes worse. Chest X-rays show widespread areas of consolidation. The patients are still salvageable in Phase III, but the mortality is high.

Phase IV: This period lasts only a few hours until death. The picture is one of progressive anoxaemia with rapidly rising lactate levels and fall in pH. Carbon dioxide retention is finally seen despite high tidal volumes, signifying greatly increased alveolar dead space. Death is due to bradycardia and asystole, secondary to anoxia.

III. Laboratory Findings

(A) *Radiological Findings in the Lung*

During Phase I, the X-ray appearance of the lungs is normal. However, as the syndrome progresses, a variety of radiological findings may be noted. Pleural effusions may be present. There are often scattered or confluent areas of increased density throughout the lung fields. There may be signs of interstitial and alveolar fluid. Atelectasis may be a prominent feature. The lung X-ray shows greater abnormality through phases II to IV, as the clinical condition deteriorates, and may be indistinguishable from that caused, for example, by severe bronchopneumonia, multiple pulmonary emboli, radiation pneumonitis, or "post-perfusion lung."[7]

(B) *Lung Pathology*

Grossly the lungs are heavy (3 to 4 times normal weight), with a high water content (greater than 80 per cent). They fill the thoracic cavity and there is little or no gross atelectasis. The lungs are dark red in colour and there is often evidence of pleural haemorrhage. On the cut surface, alveoli are reduced in size, and there are often focal areas of pulmonary haemorrhage and pneumonic consolidation.[11]

The major *microscopic* features are interstitial and alveolar oedema, with hyaline and fibrinous deposits on alveolar walls and in alveoli. It has been suggested that hyaline membrane is dried inspissated protein which has leaked from abnormally permeable capillaries.[3,8,9] Alveolar and interstitial haemorrhage, with hyperplasia and hypertrophy of the alveolar lining cells are prominent.

In normal lungs one can detect three types of lining cells: (i) membranous alveolar lining cells (Type I cells); (ii) granular alveolar lining cells (Type II cells); (iii) alveolar macrophages. In the lungs of patients who have died of the pulmonary insufficiency syndrome, there is an abnormal prominence of Type I and Type II cells, especially the Type II. There is an absolute increase in Type II

cells, and also a transformation of Type I to Type II. Type II cells are thought to be important in the manufacture of surfactant.[9]

These pathological changes are not unique to the syndrome of pulmonary insufficiency.

(C) *Pathophysiology*

The salient laboratory findings indicating pathophysiology are an increased minute volume on spontaneous respiration; decreased PaO_2 on room air; increased $A\text{–}aO_2$ difference; decreased Pco_2 eventually progressing to increased Pco_2; mixed alkalosis developing into metabolic acidosis and, terminally, mixed acidosis.

(1) *Hyperventilation*

This is one of the first signs that pulmonary problems are beginning. It lasts too long to be caused by emotion or as a response to painful stimuli. It may be caused by inadequate tissue oxygenation, in turn caused by pulmonary shunting. During low-flow states, it may be caused by under-perfusion of the chemoreceptors of the aortic arch and carotid bodies.[4]

(2) *Metabolic Alkalosis*

This is seen early in combination with respiratory alkalosis. It may be the result of (a) oxidation of citrate from massive transfusion; (b) inability of the body to excrete sodium bicarbonate derived from oxidative metabolism of sodium citrate because of (i) decreased glomerular filtration rate secondary to the low-flow state, (ii) transient hyperaldosteronism, resulting in high rates of sodium reabsorption and aciduria despite plasma alkalosis; (c) excessive removal of hydrochloric acid via nasogastric tube.

(3) *Increased A–a gradient and Shunting*

The *increased A–a gradient* is due to the interaction of three possible causes:[10] (i) limitation of oxygen transport across the blood-gas barrier, (ii) inequalities of distribution of alveolar ventilation relative to pulmonary capillary flow, (iii) true venous shunting: (a) through normal shunt channels, (b) through new or abnormal anatomic shunts, or (c) through pathological shunt channels, i.e. perfused but non-ventilated broncho-alveolar segments.[6]

Normally the true venous shunt (on breathing 100 per cent O_2) is about 3 per cent of the cardiac output and is due to blood flow through bronchial or coronary vessels which empty directly into the left heart.

Shunting Is Caused by

(i) Changes in blood-gas barrier due to alveolar and interstitial oedema, enlargement and hyperplasia of alveolar lining cells and deposition of hyaline membrane, or (ii) Alteration of blood entering pulmonary capillaries, such as: (a) High cardiac output in the post-resuscitation phase may speed up the transit time of blood through the pulmonary capillaries which would ordinarily not be perfused; for example, those which contain oedema fluid may be opened up and perfused, contributing to an increased shunt; (b) Blood entering pulmonary capillaries may be very acidotic, and will achieve a lower O_2 content at any given

O_2 tension. It may not become completely oxygenated in just one passage through the lung if the flow is rapid; (c) Perfusion of alveoli which are atelectatic or filled with fluid or hyaline membrane;[6] (d) Blockage of pulmonary capillaries with particulate matter.

In the end-stage of this syndrome, markedly impaired ventilation-perfusion imbalance leads to an increase in dead space ventilation, which causes hypercarbia. These imbalances eventually lead to the situation where one portion of the lung is being ventilated but not perfused (dead space ventilation causing hypercarbia), and the other portion is being perfused but not ventilated (shunt, causing hypoxia).

(4) *Lacticacidaemia*

Cellular hypoperfusion appears to be the most potent stimulation to the generation of excess lactate.[12] Other sources of lactic acid include (i) production by anaerobic micro-organisms, (ii) use of large amounts of electrolyte solutions containing lactate, (iii) infusion of vasopressor agents, the resulting vasoconstriction closing off the blood supply to some capillaries, and so causing anaerobic metabolism and lacticacidaemia.

(5) *Surfactant Depletion*

Interstitial oedema and damage to the surfactant layer of alveoli causes decreased compliance and increased work of breathing.

Surfactant is a lipoprotein, dipalmitoyl lecithin, attached to an alpha globulin. It is derived from the mitochondria of Type II cells. The surfactant system is essential for the maintenance of alveolar stability and normal alveolar fluid balance.[11] It may also help to regulate pulmonary capillary flow.

The pressure required to open lung units is related to surface tension by the following formula:

$$P = 2T/R$$

where P = pressure tending to resist inflation
T = surface tension
R = radius of unit

Surface tension increases during inflation and decreases (due to surfactant action) during deflation. If surfactant is disrupted, there is marked alveolar instability with collapse, and transudation of liquid into the alveolar spaces. The depletion of surfactant in the pulmonary insufficiency syndrome may be due to inadequate perfusion and oxygenation of the Type II lining cells.[12] However, it is not clear what role therapy of the syndrome (such as increased oxygen tensions in the alveoli) has in impairment of surfactant production.

IV. Pathogenesis

During the shock state changes have been noted in the pulmonary circulation.[13] There is an increase in pulmonary artery pressure and pulmonary vascular resistance, and uneven distribution of pulmonary ventilation and perfusion. Ventilation of poorly perfused respiratory units causes local hypocapnia and increased

bronchial vascular resistance. The decreased pulmonary and bronchial vascular perfusion of respiratory units may cause damage to bronchiolar epithelium, with resulting atelectasis, bronchiolitis, and pneumonitis.

In the shock state both pre-capillary and post-capillary vasoconstriction are initially present,[14] but as the condition progresses, arteriolar tone is lost, although venular vasoconstriction remains.[15] This leads to increased pulmonary capillary hydrostatic pressure and increased capillary permeability.

Figure 1 illustrates the postulated pathogenesis of refractory pulmonary insufficiency.[5]

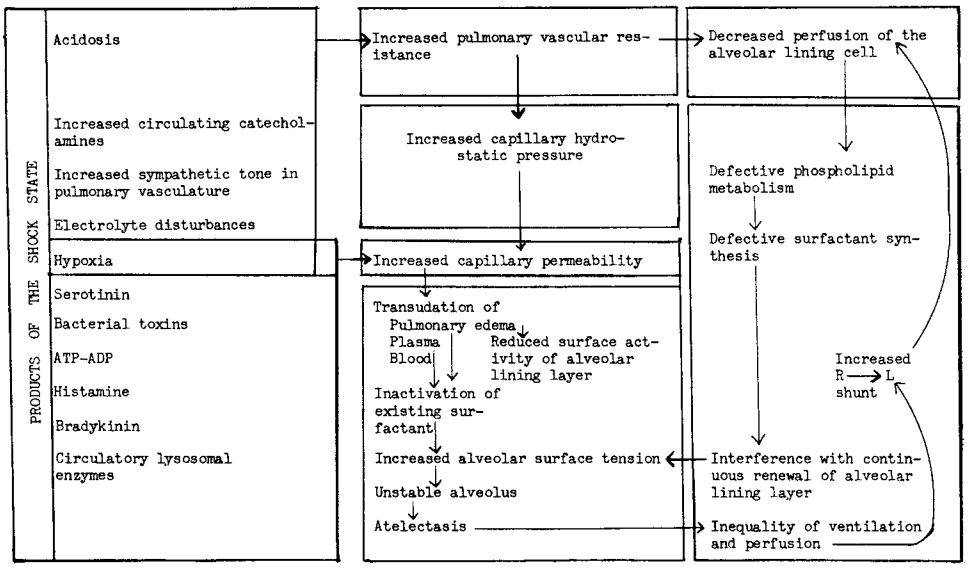

FIGURE 1. A concept of the pathogenesis of refractory pulmonary insufficiency*.

(1) *Transfusion and Fluid Overload*

Fluids transfused during and following the resuscitation period affect the lungs first before becoming diluted by body water.[16]

Fresh whole blood contains large number of white blood cells. Lymphocytes are immunologically competent and may become lodged in lung capillaries, where a graft-host reaction may be set up, damaging capillary endothelium.

Particulate matter in transfused blood may become lodged in pulmonary capillaries, causing increased shunting and increased pulmonary vascular resistance. These particles include platelet aggregates and fibrin thrombi. Serotonin is released from platelet aggregates and acts on the pulmonary microcirculation to increase pulmonary vascular resistance and contributes to bronchiolar constriction. Histamine released from sequestrated platelets may increase pulmonary vascular resistance. This is more noticeable on the venous side of the circulation.[13]

Excessive amounts of non-colloid intravenous fluids dilute the plasma proteins, thus decrease colloid osmotic pressure, and favor the transudation of fluid from capillaries into interstitial spaces.[2,17]

*After: Henry, J.N. The Effect of Shock on Pulmonary Alveolar Surfactant. J. Trauma Vol. 8, p. 765 (1968). (*Reproduced by permission*)

(2) *Fat Embolism*

Fat embolism may play a role in development of pulmonary insufficiency in the traumatic patient.[18] It is a frequent complication of fractures, especially fractures of long bones, pelvis or ribs, but it may occur after injury to other tissues containing fat.[4]

Fat droplets are freed from the cells and enter the blood stream. These are neutral fats consisting of the glycerol esters of fatty acids. The lung acts as a biological filter for this fat. In the lung these neutral fats are acted upon by lipase, produced by the lung parenchyma. The products of hydrolysis – fatty acids, and especially oleic acid, are more toxic than the neutral fats themselves, damaging capillary endothelium and diminishing lung surfactant activity.[19]

(3) *Disseminated Intravascular Coagulation (DIC) and Platelet Aggregation*

It is postulated that the prolonged hypoperfusion of peripheral tissues, such as muscle, leads to stagnation of blood in the microcirculation, diffuse intravascular coagulation with aggregation of erythrocytes and platelets and the formation of small thromboemboli.[16] These become lodged in the pulmonary microcirculation. Tissue trauma may mobilize tissue thromboplastin which contributes to the formation of intravascular coagulation. Various metabolic derangements seen in the severely injured or shocked patient may in themselves contribute to the development of DIC. Bacterial toxins in septic shock may also cause the syndrome.[5]

(4) *Aspiration*

During resuscitation unrecognized aspiration of gastric contents may occur. The accident is particularly prone to happen in severely injured patients with a distended abdomen and when in an altered state of consciousness.

(5) *Inadequate Positional Changes*

Patients lying in one position have alterations of ventilation and perfusion which are not encountered in the upright patient. Maintenance of one position, without frequent changes, favours the deposition of secretions and oedema fluid in the most dependant portion of the lung.

(6) *Oxygen Toxicity*

It is well known that oxygen in high concentration in the inspired air, for prolonged periods, is damaging to the lungs. Experiments in animals have shown that the major site of damage is the endothelium of capillaries. The pulmonary lesions produced are notable for alveolar and interstitial oedema, alveolar lining cell hypertrophy, and hyaline membrane formation. The metabolism of alveolar lining cells is interfered with, resulting in a deficiency in manufacture of surfactant, loss of compliance, and atelectasis.[16,20,21,22]

(7) *Bacterial Colonization and Antibiotics*

Infection often plays a final role in this syndrome. It does not often begin in the lung, but organisms carried by the bloodstream from other infected areas will often set up secondary infections in the already damaged tissue. Treatment with

massive doses of more than one broad spectrum antibiotic, before specific cultures and sensitivities have been carried out, contributes to overgrowth of resistant bacteria. These organisms are difficult to eradicate, and in the end stages of pulmonary insufficiency, bronchopneumonia may play a prominent role in contributing to the demise of the patient.

V. Management

The prevention of this syndrome is much more satisfactory than treatment after it has developed. Prompt restoration of blood volume and tissue perfusion in the shocked patient is most important. The clinical response to volume replacement is the major means of determining its adequacy. Monitoring of the central venous pressure (CVP) is not an infallible guide to the prevention of fluid overload. The patient may go into acute left ventricular failure with pulmonary oedema, without a rise of CVP above normal levels.[1] Blood volume determinations are of doubtful value in the acutely bleeding patient, but will be helpful in the patient without further obvious losses who does not respond with an adequate blood pressure and flow to what appears to have been adequate replacement. Excessive volumes of blood or electrolyte solutions should be avoided. The haematocrit should be maintained around 35 to 40. Values higher than this indicate increased blood viscosity, which is harmful. Blood and other intravenous fluids should be brought to room temperature and adequately filtered before delivery to the patient. The gastrointestinal tract should be kept empty through a naso-gastric tube. Frequent electrolyte and protein determinations will be a guide to fluid replacement of gastrointestinal losses. Frequent position changes are essential, as well as vigorous chest physiotherapy to promote drainage of secretions and to avoid atelectasis. The use of a strict aseptic technique when nursing the patient is important in avoiding infection. If infection develops, high doses of an antibiotic specific for the offending organism are recommended.[9] Avoid frequent changes of antibiotics.

Respiratory Management

Under the usual conditions it is difficult to achieve an inspired oxygen concentration of greater than 40 per cent with a face mask, oxygen tent or a nasal catheter. Pressure-cycled respirators, driven by oxygen, will often deliver oxygen concentrations greatly in excess of 40 per cent, while the air-mix setting is in use. Because these patients have frequent changes in compliance, volume-cycled respirators may be more reliable for treatment. This avoids frequent readjustments of the respirator to maintain adequate tidal volumes. If mechanical ventilation is going to be required for more than 24 to 48 hours, tracheostomy should be performed. Adequate humidification of all inspired gases is essential. An aseptic technique must be strictly adhered to, in care of the tracheostomized patient.

Ventilation: The carbon dioxide tension in the arterial blood is the best indicator of ventilatory adequacy. It should be about 30 to 35 Torr on controlled respiration. The patient requiring mechanical ventilation will often require increasingly large tidal volumes to maintain adequate arterial oxygen tensions. In such

cases, a dead space should be added to the equipment to prevent excessive elimination of carbon dioxide. Several "sighs", or breaths of large tidal volume, should be given each hour to prevent atelectasis. Continuous large tidal volumes may interfere with surfactant activity, and should be avoided if possible. Recently, [11,23] it has been noted that the positive expiratory pressure plateau (PEPP), brought about by having expiration occur against a resistance, will often improve the alveolar-arterial oxygen gradient. If such a technique is employed, it must be such that it does not interfere with venous return and cardiac output.

Oxygenation: During oxygen therapy every effort must be made to keep the inspired oxygen concentration as low as possible to ensure physiological arterial oxygen tension.[6] In practice, one may have to accept a Po_2 of lower than 100 Torr (70 mm Torr Hg). Adequacy of tissue oxygenation can be assessed, to a degree, by measurement of lactate levels. These should be 2 mM/L or less.

Ancillary Therapy:

(i) *Diuretics:* If fluid overload is suspected to have contributed to pulmonary insufficiency, diuretics may be useful. Therapy of the syndrome may contribute to fluid excess. It has been noted that patients on prolonged mechanical ventilation have a tendency to positive water balance, with weight gain and pulmonary oedema.[24] Etiological factors include (a) congestive heart failure (b) increased antidiuretic hormone secretion due to stimulation of left atrial volume receptors, and (c) water overload. Nebulized inspired gases may add 300 to 500 ml of fluid per day, and be overlooked in calculation of fluid balance.

Colloid solutions such as albumin may usefully be combined with diuretics, the former to draw fluid from the interstitial spaces into the intravascular compartment; the latter to promote fluid excretion by the kidneys.

(ii) *Heparin:* Heparin has been used for treatment of fat emboli as it tends to act as a "clearing factor" for fat-laden plasma. However, it is likely more useful in blocking the release of serotonin and other amines from platelets.[5] Its use in fat embolization remains controversial. Heparin is useful in proven cases of D.I.C., by partially inhibiting platelet adhesiveness and aggregation. It also inhibits the organization of platelet emboli into more permanent thromboemboli.[5]

(iii) *Adrenocorticosteroids:* Adrenocorticosteroids have been used on a somewhat empiric basis to combat alveolar oedema.[11] They will also reduce bronchoconstriction if this is a component of the syndrome. They tend to block the inflammatory reaction associated with the chemical phase of fat embolism.[19,25]

Summary

Progressive respiratory insufficiency is known to be a disturbing complication following initial therapy for shock or trauma. The syndrome has been divided into four clearcut phases, with initial hypocapnia and associated metabolic acidosis. In the end stage, hypercapnia is present as well, and death is due to asystole secondary to anoxia.

Radiological findings are non-specific. Pathologically oedema, hyaline and fibrinous deposits, haemorrhage and hyperplasia of alveolar lining cells may be seen.

The major pathophysiological features include persistent hyperventilation, metabolic alkalosis progressing to metabolic acidosis secondary to tissue hypoxia, an increased alveolar-arterial oxygen gradient with greatly increased shunting through the lungs. Some of the proposed mechanisms for shunting are discussed, including surfactant depletion.

The pathogenesis of the syndrome is unknown, but several aetiological factors have been proposed. These include fluid overload, fat embolism, platelet aggregation and disseminated intravascular coagulation, aspiration, inadequate position changes, oxygen toxicity and bacterial colonization.

Prevention of the syndrome is more successful than its therapy. Early recognition and treatment of respiratory problems are important.

Management tends to be supportive and often empirical. Avoidance of overtransfusion, adequate ventilation with carefully-controlled inspired oxygen concentrations, strict asepsis, diuretics and corticosteroids may play a role. In spite of our best efforts, the mortality of respiratory insufficiency following shock or trauma remains high.

Résumé

Il est bien établi que l'insuffisance respiratoire progressive est une complication fréquente qui s'installe après la phase aiguë du choc ou des grands traumatismes. Ce syndrome se divise en quatre phases bien distinctes. Au début nous sommes en présence d'une hypocapnie et d'une acidose métabolique. Nous voyons apparaître par la suite une hypercapnie et une mort par asystolie anoxique.

Les signes radiologiques ne sont pas spécifiques. A l'autopsie, on trouve de l'œdème, des dépots hyalins et fibrineux. Des hémorragies et une hyperplasie des cellules alvéolaires peuvent être rencontrées.

Les principaux faits pathophysiologiques sont une hyperventilation persistante, une alcalose métabolique qui se change en acidose à la suite de l'anoxie tissulaire, une différence alvéolo-artérielle qui grandit à cause du shunt au niveau pulmonaire. Les mécanismes de ce shunt ont été discutés, la disparition du surfactant inclusivement.

La pathogénèse de ce syndrome est inconnue, cependant plusieurs causes ont été proposées. Elles incluent la surcharge liquidienne, les embolies graisseuses, l'aggrégation plaquettaire, la coagulation intravasculaire disséminée, l'aspiration, l'immobilisation, la toxicité de l'oxygène et la colonisation bactérienne.

La prévention de ce syndrome a plus de succès que son traitement. L'élimination des surcharges transfusionnelles, la ventilation adéquate avec des concentrations contrôlées d'oxygène, une asepsie stricte, les diurétiques et les corticoïdes sont bénéfiques. Malgré les soins les plus attentifs, la mortalité par insuffisance respiratoire à la suite du choc ou des grands traumatismes demeure élevée.

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