



# Whole Lung Lavage

# 45

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## Key Points

- Patients with pulmonary alveolar proteinosis have a restrictive disease and are hypoxic.
- Lavage of one lung with large quantities of saline requires careful lung isolation.
- For more than 10 years, bilateral lung lavage has been performed during the same anesthetic period.
- GM-CSF is now a complementary treatment to whole lung lavage when needed.

## Introduction

This chapter reviews the historical considerations of whole lung lavage (WLL), when its performance is appropriate, details of the technique, complications, and finally benefits of this unusual treatment modality. It is important to differentiate WLL from bronchoalveolar lavage (BAL). BAL is a diagnostic tool performed with the aid of a fiberoptic bronchoscope (FOB) under local anesthesia, which uses only 300 mL of liquid in one segment of the lung. WLL is a treatment modality that requires over 10 L of normal saline instilled through a double-lumen tube in one whole lung while the patient is under general anesthesia.

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## Historical Consideration

WLL was first described in 1928 [1]. In the early 1960s, the first application of this technique was used to treat pulmonary alveolar proteinosis (PAP) [2–5]. At that time, the procedure consisted in repeated segmental flooding through a percutaneous transtracheal catheter positioned blindly into the bronchial tree. This technique was performed in an awake patient and was repeated four times a day for 2–3 weeks, using physical positioning to direct the saline sequentially into different lung segments. The 1980–2000 period led to the development of a modern technique of unilateral WLL, which is carried out under general anesthesia and lung separation [6, 7]. Since the beginning of this century, performing bilateral WLL during the same anesthesia period is the gold standard. In parallel with this evolution, the pathogenesis of WLL has been better defined since the discovery of the role of granulocyte-macrophage colony-stimulating factor (GM-CSF) in surfactant catabolism.

## Indications

WLL is the most effective proven treatment modality for symptomatic pulmonary alveolar proteinosis [1, 2]. Various pathologic states have been also treated by WLL including cystic fibrosis, asthma, chronic obstructive lung disease, radioactive dust inhalation, alveolar microlithiasis, lipid pneumonitis or exogenous lipid pneumonia, and silicosis with variable success [8].

## Pulmonary Alveolar Proteinosis

Primary pulmonary alveolar proteinosis (PAP) is a rare disorder of unknown cause and variable natural history. This lung disease is caused by alveolar accumulation of a lipoprotein material that has the aspect of surfactant. This accumulation of material creates a true alveolo-capillary blockade,

and the patient presents with dyspnea and hypoxemia, aggravated by exercise.

### Pathogenesis and Classification

Until recently, the pathogenesis of PAP was unknown. Most investigators have postulated a decreased clearance of surfactant from the alveolar space. Over the last decade, rapid progresses were made toward the elucidation of the molecular mechanisms of PAP. Recent data suggest that GM-CSF has a pivotal role in PAP pathogenesis, as it is required for normal surfactant homeostasis. The disease is associated with neutralizing autoantibodies against GM-CSF. This new information allows the development of a new classification for this orphan lung disease and the use of new therapies. Some studies have been conducted with inhaled and subcutaneous GM-CSF. The latter form shows improvement in oxygenation and quality of life in 48% of patients [9]. The main conclusion is that GM-CSF treatment appears to benefit a subset of patients with adult PAP and may represent a novel alternative to the repeated whole lung lavages.

Three forms of PAP are now recognized: primary, secondary, and congenital [10]. The primary (idiopathic) form of PAP is the most common disease presentation, representing more than 90% of all cases. Its onset occurs in adulthood, and it has an autoimmune origin. It is associated with a high prevalence of circulating anti-GM-CSF antibodies. Reduction of localized GM-CSF activity in the lung, secondary to the presence of neutralizing anti-GM-CSF antibodies, causes alveolar macrophage dysfunction, resulting in surfactant excess and accumulation [11]. There is no other associated underlying illness or exposure.

The secondary form also develops in adulthood, occurs with other conditions, and can be separated into two broad subgroups. These are systemic inflammatory diseases or malignancy and specific exogenous exposure. Exposure to a high level of inorganic dusts (e.g., silica, aluminum, titanium, cement, wood) or fumes (chlorine, gas, gasoline, plastics) has been incriminated. Secondary PAP is likely related to a relative deficiency of GM-CSF and related macrophage dysfunction.

The congenital form is often present in the neonatal period and results from a very rare gene mutation. This mutation is related to the surfactant receptor gene or to the GM-CSF gene. This form is rare but is usually very severe. Neonatal respiratory distress syndrome is a presentation form of congenital PAP.

### Clinical Manifestations

Among adults, the typical age of apparition of the illness is 30–50 years. There is a male to female ratio of 2:1. The major symptom of PAP is a progressive dyspnea and hypoxemia on exertion, spread over months and sometimes years. Dyspnea, the most common presenting symptom, is reported by approximately 55–80% of patients; however, approximately one-third of affected patients are asymptom-

atic, despite the infiltration of the alveolar air space. Nonproductive cough, fatigue, weight loss, and low-grade fever have also been described.

Spontaneous remission can occur, but the therapeutic decision in PAP depends on the progression of the illness and the extent of the physiological impairment. The prognosis of PAP has greatly improved since the introduction of WLL by Ramirez in 1965. The usual objective of WLL is the improvement in the clinical, physiological, and radiological condition of the patient.

### Radiographic Findings

Chest radiography is the most useful screening test, although very nonspecific [12, 13]. On chest radiography, bilateral symmetric alveolar opacities located centrally in mid- and lower or upper lung zones are typical, yielding a “butterfly” distribution. High-resolution CT scanning (HRCT) reveals ground-glass opacification, predominantly in a homogeneous distribution. Thickened intralobular structures and interlobular septa in typical polygonal shapes may also be observed, referred to as “crazy paving.” Crazy paving is characteristic but not specific to PAP and can also be observed in patients with an acute respiratory distress syndrome, lipoid pneumonia, acute interstitial pneumonia, drug-related hypersensitivity reactions, and diffuse alveolar damage superimposed on usual interstitial pneumonitis [14].

### Physiological Testing

Pulmonary function tests show a restrictive ventilatory defect with reduction in the total lung capacity and vital capacity. When present, the decrement in diffusing capacity for carbon dioxide (DLCO) is often out of proportion to the degree of the restrictive defect. Arterial blood gas analysis shows mild to moderate hypoxemia, with an elevated alveolar-arterial gradient and elevation in shunt fraction while breathing 100% O<sub>2</sub> [15].

### Laboratory Investigation

Bronchoalveolar lavage (BAL) may help in establishing the diagnosis in clinically suspected cases. BAL fluid is opaque and presents a “milky” appearance, with large amounts of granular, acellular eosinophilic lipoproteinaceous material which is periodic acid-Schiff (PAS). Electron microscopic exam of BAL fluid can confirm the diagnosis [16, 17]. When allowed to stand, the fluid spontaneously separates into pale yellow, almost translucent supernatant, and thick sediment.

Obtaining tissue for histopathology by open lung biopsy has been the gold standard for a long time. This biopsy performed by VATS is now unnecessary in the majority of cases of PAP. The combination of the clinical presentation, imaging findings, and BAL results are generally sufficient to make the diagnosis. Transbronchial biopsies may be occasionally used when needed. Surgical lung biopsy is rarely necessary to make the diagnosis [18–20].

Furthermore, anti-GM-CSF antibodies are increasingly used as a diagnostic tool in PAP. The quantitative assessment of anti-GM-CSF antibodies in reference laboratories constitutes an important diagnostic and therapy-guiding measurement [21]. GM-CSF antibodies are present in all serum and BAL fluid samples from primary, idiopathic, PAP patients. BAL fluid levels of anti-GM-CSF antibodies correlate better with the severity of PAP compared to serum titers [22]. Serial measurements of BAL or serum anti-GM-CSF antibodies may be useful in monitoring disease activity and response to treatment.

### Therapy

The treatment depends on the form of PAP. When dealing with idiopathic PAP, the use of WLL, GM-CSF, rituximab (Rituxan®), or plasmapheresis (see later) can be considered. For secondary PAP, treatment of the underlying condition or removal of the offending agent should be the first step to consider. When confronted with congenital PAP, WLL, supportive therapy, or lung transplantation is the ultimate treatment.

### Whole Lung Lavage

Treatment of idiopathic PAP has evolved from the use of a variety of nonspecific and largely ineffective agents to the physical removal of the lipoproteinaceous material from the lungs (WLL) and to the development of specific therapy targeting the underlying pathogenesis of the disorder. WLL has, for a long time, been considered the definitive therapy for PAP. The idea that the accumulated material could be physically removed from the lungs of PAP patients was first advanced in the early 1960s.

Specific indications for lung lavage include a definitive histological diagnosis and one of the following: resting  $\text{PaO}_2 < 65$  mmHg, alveolar-arterial  $\text{O}_2$  gradient  $\geq 40$  mmHg, measured shunt fraction  $>10$ – $12\%$ , severe dyspnea, and hypoxemia at rest or on exercise. It is critical not to perform WLL when a patient has active bacterial pneumonia, since this can result in generalized sepsis and shock [11].

Physical removal of the lipoproteinaceous material through repeated dilutions with saline solution is believed to be the mechanism from which WLL shows benefits; additional mechanisms including the bulk removal of anti-GM-CSF antibody, as well as other possible immunologic effects on the effector cells, such as the alveolar macrophage or the type II epithelial cell, are possible [23].

Although fairly well tolerated, WLL sometimes only provides temporary symptomatic benefit and has then to be repeated several times. The lavage requires prolonged general anesthesia, is complex to perform, and is associated with potential morbidity. All these considerations make repeated WLL a less-than-desirable treatment. Hence, the search for alternative modalities of therapy is still crucial.

### GM-CSF

Discovery of the alveolar macrophage involvement and anti-GM-CSF neutralizing antibodies led to multiple trials examining the usefulness of GM-CSF therapy. Preliminary data suggest that about 48% of patients treated with subcutaneous GM-CSF experienced improvement in pulmonary symptoms and function; however, the number of respondents appears to be less than with whole lung lavage. Given the experimental nature of GM-CSF therapy, the use of lung lavage is still the primary therapy for PAP.

Inhalation of nebulized GM-CSF has also been reported to improve lung function and facilitate clearance of the GM-CSF-antibody complexes from the lung. Additionally, a recent study using a two-pronged approach showed a decrease in GM-CSF requirements by performing WLL followed by nebulization of GM-CSF. It also appears that high amounts of exogenous GM-CSF can overcome the endogenous neutralizing antibodies, especially if GM-CSF is directly administered to the lung. This result would seem to be explained by the lipoproteinaceous material cleared by WLL, and consequently the inhaled GM-CSF could more readily reach the alveoli [11].

Although the positive effect of GM-CSF has been shown in idiopathic PAP, many important questions remain, including the optimal dose of GM-CSF, the optimal duration of treatment, the relation to the anti-GM-CSF titers, and the optimal route of GM-CSF administration.

### Other Therapies

Rituximab (Rituxan®) is a monoclonal antibody directed against B lymphocytes. Since 1997, rituximab has been demonstrated to be effective in various autoantibody-mediated diseases like PAP [24]. Treatment with plasmapheresis to decrease the level of GM-CSF antibodies has yielded mixed results [25, 26]. Lung transplantation has been performed in patients whose health has deteriorated despite multimodal therapy, but recurrence in the allograft has been reported [27].

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## Whole-Lung Lavage Technique

In the author's quaternary center, the team is composed of trained and experienced staff consisting of two respiratory therapists, one nurse, two physiotherapists, and one anesthesiologist in charge of the anesthesia and of the lung lavage [7] (Table 45.1).

### Monitoring

Whole lung lavage is realized under general anesthesia with basic monitoring, supplement respiratory monitoring, and sometimes invasive monitoring. In addition to the standard monitoring devices, an arterial cannulation is used for

**Table 45.1** Whole lung lavage – proceeding

Stages	Whole lung lavage – proceeding
1	<i>Induction of anesthesia</i> Insertion of the left DLT with carinal hook
2	<i>Pre-lavage evaluation</i> (FiO <sub>2</sub> 1) Conventional ventilation for 5 min → arterial blood gas (ABG) Left OLV for 5 min → ABG Right OLV for 5 min → ABG
3	<i>First lung lavage</i> Lung lavage on the lung with the worst PaO <sub>2</sub> on OLV Multiple lavage/drainage cycles Fifth cycle done in lateral decubitus position * Contamination risk on the dependent lung Following fifth cycle: manual ventilation halfway through drainage phase End of cycles when the drainage fluid returns clear Aspiration with soft suction and FOB
4	<i>Recovery/lung rest</i> Protective 2 lung ventilation TV 6–8 mL/kg, PEEP 7–12 cmH <sub>2</sub> O, FiO <sub>2</sub> < 0.6 if well tolerated Fluid balance and diuretics if needed Cover the patient with heating blanket Length: 30–45 min
5	<i>Preparation for second lung lavage</i> (FiO <sub>2</sub> 1) OLV on the fresh lavaged lung for 5 min → ABG If PaO <sub>2</sub> > 70 mmHg Proceed with the 2nd lung If PaO <sub>2</sub> < 70 mmHg Consider adjuvants (iNO, PAC) Report proceeding with the 2nd lung
6	<i>Second lung lavage</i> Idem as the first lavage
7	<i>Landing phase</i> Replace the DLT by a single-lumen tube Aspiration with soft suction and FOB
8	<i>Emerging phase</i> Protective ventilation (2–4 h) in a monitored unit Post-anesthesia care unit Intensive care unit ABG and chest X-ray Awakening and extubation
9	<i>Observation phase</i> 24 h in a monitored unit ABG and chest X-ray evaluation <i>Noninvasive positive-pressure ventilation as needed</i>

beat-to-beat measurement of blood pressure and for blood gases analysis. Some authors also suggest the use of pulmonary artery catheter, continuous monitoring of mixed venous oxygen saturation [28, 29], and transesophageal echocardiography (TEE) [30, 31]. The pulmonary artery catheter may be used more as a therapeutic aid than a monitoring device by diverging blood flow away from the lavaged lung. TEE is sometimes useful to evaluate the cardiac function, mainly the right ventricle, in the presence of pulmonary hypertension.

The ventilator monitor found on most new anesthesia machines provides essential information during the

WLL. The observation of the airway pressure/volume loop (spirometry) on a breath-to-breath basis is useful to detect any loss of lung isolation and to prevent flooding of the ventilate lung [7, 32].

## General Anesthesia

Only light premedication with anxiolytic drugs is used. Efficient preoxygenation is mandatory. General anesthesia is induced and maintained with intravenous agents, such as narcotics, benzodiazepine, intravenous anesthetic, and muscle relaxants. Inhaled anesthetic is rarely used. Minimal intravenous hydration is administered since many liters of fluids originating from the alveolar space will be reabsorbed into the vascular space. Usually, the procedure for unilateral lavage lasts between 3–4 h and 5–6 h for a bilateral lavage. The use of a warming blanket over the legs helps to minimize heat loss as the thorax is completely denuded for the procedure.

## Lung Separation

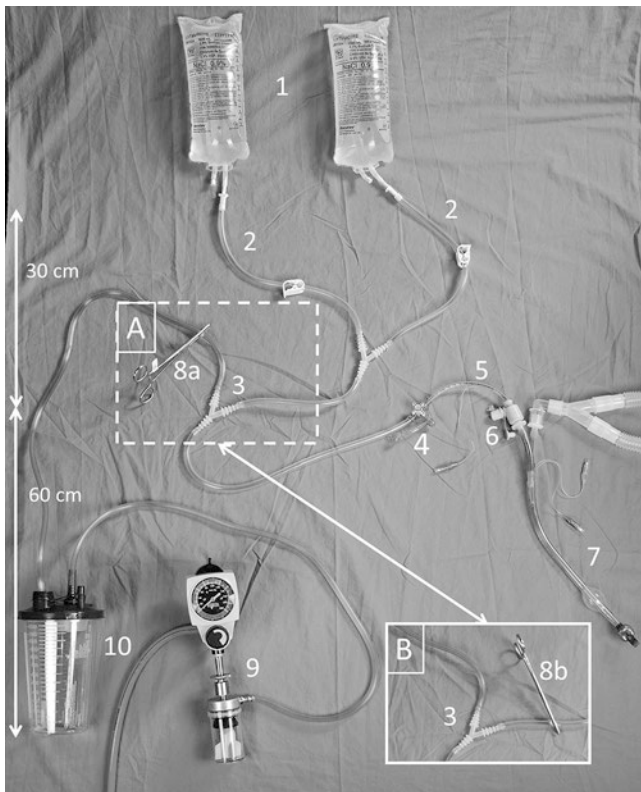
Lung separation is obtained by using a disposable left double-lumen tube (DLT). For the purpose of WLL, a left DLT with a carinal hook is used. The carinal hook offers a better stability of the tube given the numerous manipulations that occur during lung lavage. Adequate positioning of the DLT is achieved by the use of FOB, and air tightness is confirmed by a well-closed pressure-volume loop. Gas exchanges are obtained from both lungs simultaneously and then from each lung separately before and after the procedure to measure the effects of the WLL objectively.

## Lung Lavage

The patient is kept in the supine position. To improve the effectiveness of the lavage, ventilation with FiO<sub>2</sub> 1.0 is initiated for a few minutes to denitrogenate both lungs. Pre-lavage evaluation confirms which lung is the most impaired, mainly through imaging evaluations and blood gas exchange during bilateral sequential one-lung ventilation (OLV). The most impaired lung is the first to be lavaged.

OLV is instituted in the non-lavaged lung, and confirmation of perfect lung isolation is obtained from the spirometry loop. A homemade disposable irrigation and drainage system (Fig. 45.1) is used to instill approximately 1 L of warm normal saline (37 °C). The irrigating liquid is suspended 30 cm above the patient's mid-chest level, and the instillation takes about 2–5 min.





**Fig. 45.1** Irrigation and drainage system. (1) Normal saline bag, (2) large bore tubular set for bladder irrigation, (3) Y-adaptor, (4) three-way for enteral feeding, (5) 5.0 mm single-lumen endotracheal tube, (6) swivel adaptor, (7) double-lumen endotracheal tube, (8a) clamp on the drainage side tubing during instillation phase, (8b) clamp on the instillation side tubing during drainage phase, (9) suction unit, (10) suction bottle. (Reproduced with permission of Libbey [52])

Approximately 2 min after the lung is completely filled with saline, it is rapidly drained over a 5–10 min period into a container positioned 60 cm below the patient's mid-chest level, with the assistance of a low suction pressure level (<20 cm H<sub>2</sub>O). This process is repeated ten times or more, as necessary, to obtain a clear effluent lavage fluid.

Mechanical maneuvers are used to increase the efficacy of the WLL. These techniques consist of manual chest physiotherapy, mainly percussions, vibrations, and pressure applied during the filling and the drainage phase [33, 34]. A flannel cloth is used to protect the patient's skin from irritation provoked by repetitive manipulations. Positional modifications are very useful to irrigate and to drain all the different segments of the lung. The full lateral position is used at least once during the procedure, usually at the fifth cycle. When the lavaged lung is up, extreme care must be taken to avoid the risk of leakage from this nondependent lavaged lung into the dependent and ventilated one. After six or seven cycles of lavage and drainage, manual ventilation of the lavaged lung is frequently used halfway during the drainage phase to help the evacuation of the alveolar material

[35]. When the effluent lavage fluid is clear, the procedure is completed.

### Bilateral WLL

For more than 15 years, bilateral WLL is done during the same anesthetic period and is performed with good results. Before bilateral WLL was performed in the same anesthetic episode, it was initially performed on the sickest lung; then at least a week later, the WLL of the contralateral lung was completed. At that time, oxygenation was usually not a problem because the treated and now near-normal lung was used to support gas exchange during the second procedure. We realized, with the experience of the bilateral WLL, that the lung recuperates rapidly enough to allow the contralateral WLL in less than an hour after the initial one.

When the effluent lavage fluid is clear on the first lavaged lung, careful aspiration is done, blindly with a suction catheter and also under direct vision with the use of a FOB. In order to safely proceed with WLL on the contralateral lung, a recuperation period has to be respected for the recently lavaged lung. Both lungs are ventilated with normal tidal volume (8–10 mL/kg) with addition of PEEP at a level varying from 7 to 12 cmH<sub>2</sub>O for a period of 30–45 min. Furosemide can be administered (10 mg) to induce diuresis during this period, and patient's body is entirely covered with a warming blanket to keep its temperature close to normal.

Following determination of the ability of the recently lavaged lung to support the OLV necessary for the lavage of the contralateral lung, another WLL is done as previously described. Our goal is to obtain a PaO<sub>2</sub> greater than 70 mmHg with a FiO<sub>2</sub> 1.0, with or without PEEP prior to begin WLL. When a satisfactory oxygenation cannot be achieved, inhaled nitric oxide is used at 20 ppm, and/or a pulmonary artery catheter is inserted under fluoroscopy in order to diverge blood flow from the lavaged lung to the ventilated lung [36]. When the adequacy of oxygenation is demonstrated, the WLL on the second lung is performed similarly to the first one.

### Associated Bronchoalveolar Lavage (BAL)

In some specific cases, when the distribution of the alveolar infiltration is not homogeneous and is more localized into some specific lobes, the author adds to the standard WLL a series of BAL, well directed to the main involved lobes. BAL is performed after the WLL, following the exchange from DLT to a large, over 8 mm, single-lumen endotracheal tube. A regular FOB is used to obtain a bigger suctioning channel. BAL is performed at the segmental level. A maxi-

imum of 150 mL aliquots of normal saline is injected, followed by a drainage period assisted by the same system as the one used during regular WLL. BALs are repeated as needed, that is, until the return of clear liquid from the treated lobe. Every involved lobe is lavaged with the same technique.

## Complications

The main complication is a decrease in arterial oxygen saturation, mainly during the drainage phase. Some liquid spillage from the lavaged lung to the non-lavaged lung may also occur. Other complications such as pneumothorax and hydrothorax are rare but may need to be drained, resulting in a postponed procedure. Post-procedure complications are pneumonia, sepsis, and, rarely, acute respiratory distress syndrome.

## Desaturation

Increase in the blood flow in the non-ventilated lung occurs during the drainage phase (Fig. 45.2). This causes a decrease in arterial oxygen saturation. The use of PEEP on the ventilated lung helps to improve oxygenation during the filling phase but may worsen the PaO<sub>2</sub> during the drainage phase [37]. At that time, if needed (low SatO<sub>2</sub>, i.e., <80% and/or for a prolonged period), a temporary partial unilateral pulmonary artery balloon occlusion with a pulmonary artery catheter, positioned under fluoroscopy in the artery of the lavaged lung, may be used. The occlusion diverts blood flow from the lavaged lung to the ventilated lung to improve oxygenation [36]. The use of nitric oxide with or without almitrine infusion has been described [38]. Others have performed the whole lung lavage under hyperbaric conditions [39]. Sometimes the patient presents severe impairment in gas exchange not allowing OLV. At that time, the use of venovenous or venoarterial extracorporeal membrane oxygen-

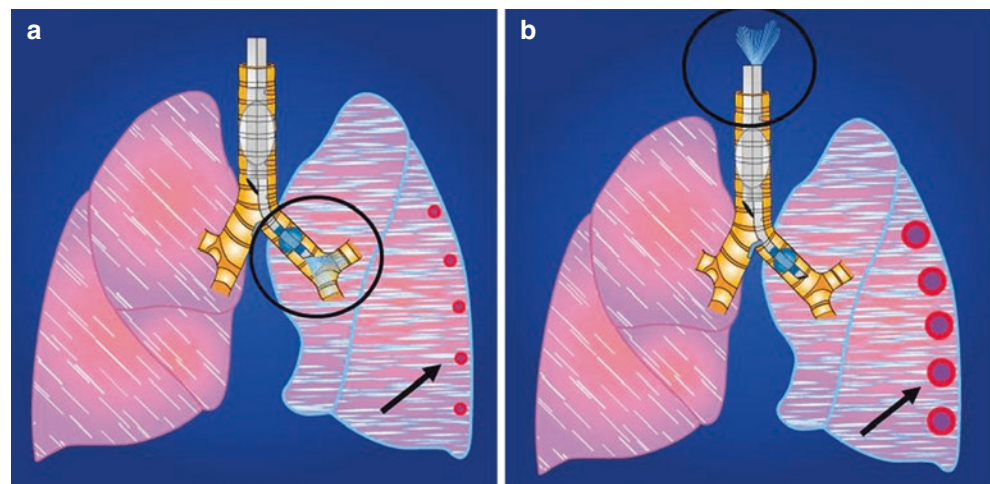
ation (ECMO) or cardiopulmonary bypass (CPB) is useful to avoid severe hypoxemia during OLV [40]. The use of an extracorporeal membrane oxygenator has been also described to perform bilateral simultaneous whole lung lavage [41–43]. The use of a hyperoxygenated solution has been investigated. Its use improved oxygen supply in comparison to normal saline, as lavage solution, without obvious side effects [44].

## Leakage

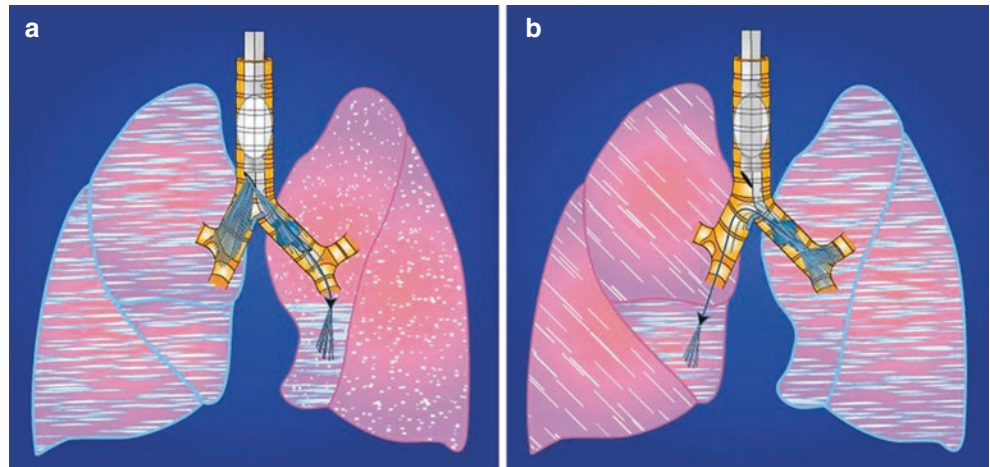
Spirometry must be used continuously to monitor and diagnose any liquid spillage from the lavaged lung. The mechanism of liquid spillage differs depending on which side the lavaged lung is lying (Fig. 45.3). When the whole lung lavage is performed in the right lung with a left-sided DLT in place, overpressure comes from the trachea over the bronchial balloon. When leaking occurs, there is flooding of the left ventilated lung. When it is happening during lavage of the left lung, leaking is caused by an overpressure in the left lung over the bronchial balloon or from a proximal displacement of the DLT. It creates leakage from the left lung to the trachea and finally to the right ventilated lung.

If there is a modification of the aspect of the spirometry loops, it is important to suspect flooding of the ventilated lung. At that time, it is essential to stop the irrigation or to increase the drainage, depending on timing. Confirmation by FOB and treatment by vigorous suctioning and inflation of the involved lung should be performed. It is essential to assess the non-lavaged lung function before continuing the lavage to ensure that the flooded lung can provide adequate oxygenation during subsequent one-lung ventilation. In the context of unilateral WLL, when flooding of the non-lavaged lung occurs, it frequently requires prolongation of ventilation during the post-procedure period to allow recovery. The best treatment for this complication is prevention, which can be done with a secure fixation of the double-lumen tube, the use of a double-lumen tube with a carinal hook, and by being

**Fig. 45.2** Desaturation. (a) During the filling phase (circle), there is reduction of blood flow to the non-ventilated lung, by compression of the pulmonary blood vessels (arrow). (b) During the drainage phase (circle), there is reperfusion of the non-ventilated lung (arrow), creating a shunt and leading to desaturation. (Reproduced with permission of *Anesthesiology Clinics of North America* [7] (September 2001))



**Fig. 45.3** Leakage from the lavaged lung to the non-lavaged lung. (a) During right lung lavage, overpressure in the trachea provokes flooding in the left ventilated lung. (b) During left lung lavage, overpressure in the left lung or displacement of the DLT provokes flooding of the right ventilated lung. (Reproduced with permission of *Anesthesiology Clinics of North America* [7] (September 2001))



**Fig. 45.4** Fluids collected from whole lung lavage. Fluids collected from WLL in pulmonary alveolar proteinosis seem milky. When fluid lavages are allowed to stand for a few hours, thick sediment appears in

the bottom of the collecting bottle. It is more abundant in the first bottles going to near zero in the last ones. (Reproduced with permission of *Anesthesiology Clinics of North America* [7] (September 2001))

careful not to dislodge the double-lumen tube during patient and head manipulations.

## Ending

The end point that is clinically used to cease a lung lavage is when the effluent lavage fluid is clear. Usually, between 10 and 15 L of saline are instilled into each lung (up to 50 L), and more than 90% of this volume is recovered, leaving a recuperation deficit of less than 10%. At the end of the procedure, the lavaged lung is thoroughly suctioned, and the volume of the residual liquid aspirated is calculated in a strict “in and out” balance of lavage liquid.

The effluent liquid of the whole lung lavage looks different depending on the pathology being treated. The sediment may seem milky following WLL for PAP (Fig. 45.4), while it may appear sandy if lung lavage is performed for silicosis. Over the past few years, the author has evaluated the amount of sediment recuperated during WLL for each lung separately (Fig. 45.5). The sediment amount is determined after fluid lavages are allowed to stand for at least

2–3 h. Then, the fluid spontaneously separates into a translucent supernatant and a thick sediment. The total height of sedimentary deposition in all the suction bottles allows quantifying the effectiveness of WLL in each lung individually. The accumulation may vary from 50 to 150 mm for each lung, meaning up to 300 mm following bilateral WLL.

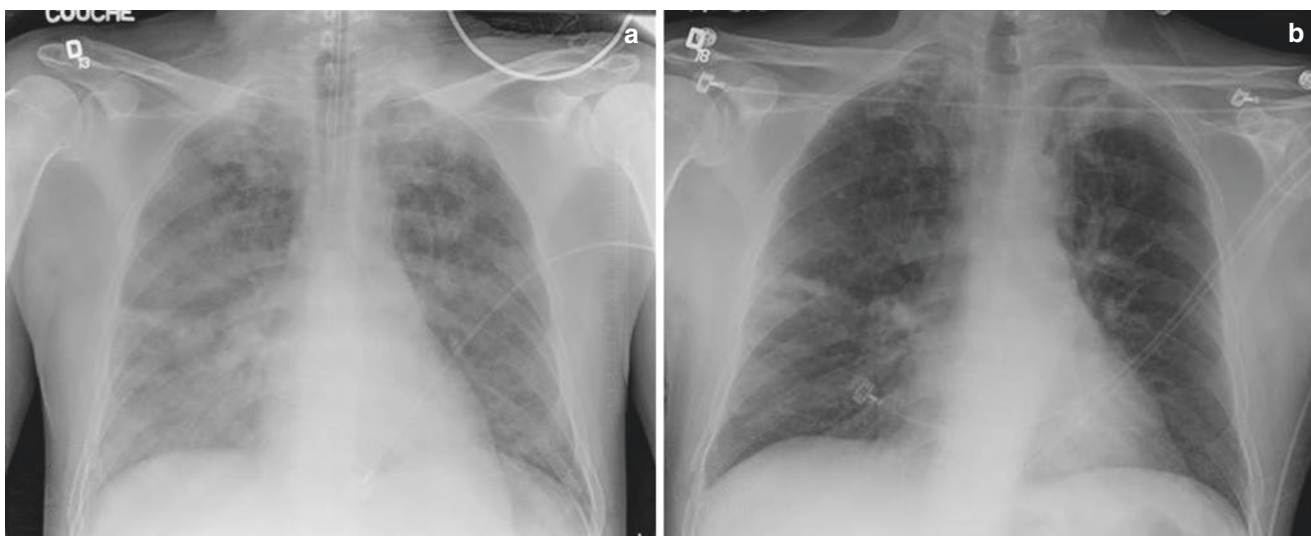
After reintubation with a single-lumen endotracheal tube, a fiberoptic bronchoscopy control inspection is performed to look for the occurrence of undetected leakage throughout the procedure. During the FOB inspection, the author regularly observes local irritation of the distal tracheal mucosa, secondary to the movement of the double-lumen tube during WLL. The use of a double-lumen tube with a carinal hook has noticeably decreased the incidence of this irritation.

Conventional ventilation with PEEP is continued, usually for less than 2–4 h, to restore lung function, until the patient awakens in the recovery room. Alveolar infiltrates seen on the chest X-ray immediately after WLL normally clear within 24–36 h (Fig. 45.6). Observation in the ICU for 24 h is part of routine procedure.





**Fig. 45.5** Sediment measurement. Total height of sedimentary deposition in all the suction bottles allows quantifying the effectiveness of whole lung lavage in each lung individually



**Fig. 45.6** Radiological imaging. (a) Immediately after left whole lung lavage, note the important alveolar edema resulting from the procedure. (b) The day after the right-side whole lung lavage, note the important amelioration of the two lungs. (Reproduced with permission of Springer)

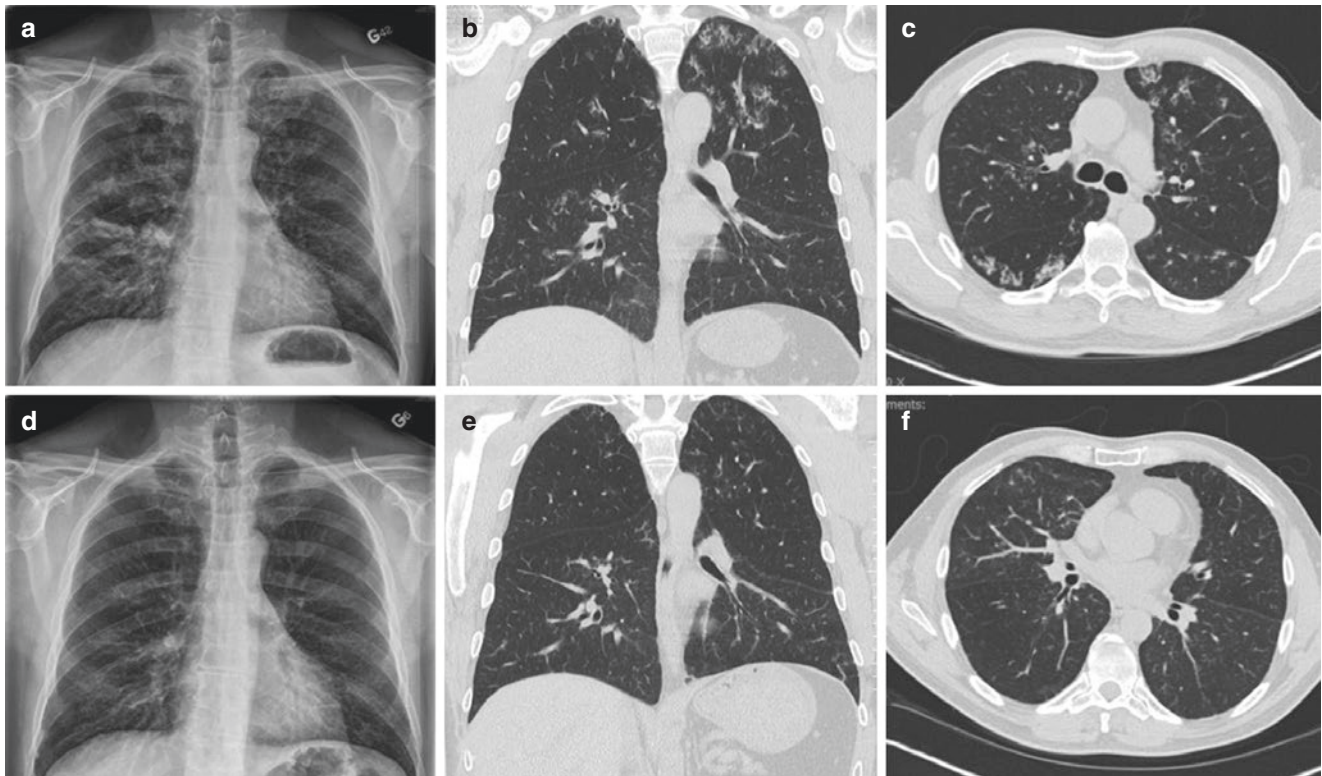
### Post Whole-Lung Lavage Evolution

The impact of WLL on the natural history of idiopathic PAP is difficult to ascertain, given the absence of randomized prospective trials or large, long-standing registries. However, practitioners of this procedure widely believe that patients with PAP improve symptomatically due to better gas exchanges. After whole lung lavage, patients usually have marked subjective improvement that correlates with increases in PaO<sub>2</sub> (at rest and exercise), vital capacity, diffusing capacity, and clearing of the chest roentgenogram (Fig. 45.6) or CT-scan (Fig. 45.7). Some patients require lavage every few months, whereas others remain in remis-

sion for several years. The disease may eventually show late recurrence. In PAP, WLL is proven to be successful because the lavage removes enormous accumulations of alveolar lipoproteinaceous material but also probably because it interrupts the pathogenic loop, decreasing the level of anti GM-GSF at the alveolar site, and temporarily restores the activity and function of the macrophages. It should be noted that congenital PAP appears to be particularly unlikely to respond to WLL [18].

An excellent retrospective review of all published articles, describing over 400 individual cases of PAP, was published in 2002 by Seymour and Presneill [18]. They reported that 41 patients with pre-lavage and post-lavage paired gas exchange results have seen their PaO<sub>2</sub> improved by





**Fig. 45.7** Radiological imaging before (a–c) and following (d–f) whole lung lavage and GM-CSF by inhalation. (a) Anteroposterior view demonstrating the heterogeneous radiological infiltrations. They are mainly localized in the left superior lobe and the supero-dorsal segment of the bilateral inferior lobes. (b) High-definition computed tomography scan, coronal plane, showing the same involvement. (c) High-definition computed tomography scan, axial plane, showing

crazy paving imaging in the left upper lobe. (d) Anteroposterior view demonstrating the disappearance of radiological infiltrations. (e) High-definition computed tomography scan, coronal plane, showing the same improvement. (f) High-definition computed tomography scan, axial plane, showing that the alveolar material has cleared out compared to c. (Reproduced with permission of Springer [53])

20 mmHg following WLL. The improvements in other pulmonary function parameters or diffusing capacity were less impressive. Their results also indicate that the median total number of lavages performed was two and that the median symptom-free period after one session of WLL was 15 months.

With regard to survival, in their analysis of the literature, Seymour and Presneill indicated that the overall survival at 5 years from the time of diagnosis is higher for patients who underwent therapeutic lung lavage during the course of their disease (94% vs. 85%, for those not lavaged). This was based on a series of 146 patients who were lavaged and 85 patients who were not [18].

### Pediatric Whole Lung Lavage

Whole lung lavage has been used in the pediatric and neonatal population with some success. Whole lung lavage is technically difficult in infants and small children because of the incapacity to ventilate part of the lung or one lung safely and adequately during lavage of other areas or the other lung.

Small double-lumen tube (Bronchopart®, size 26, 28, and 32, Willy Rusch AG, 71394 Kernen, Germany or Broncho-Cath® size 28 and 32, Mallinckrodt Medical, Athlone, Ireland) is now available for use in children aged over 8–10 years old or weighing over 30 kg. Small FOB are also available to verify and adjust the final position of the DLT. When the airway of a child accepts a DLT, the WLL technique is similar to the one performed in adults.

If the airway is too small to insert a DLT, WLL is technically more challenging. Different methods to isolate both lungs have been described [45, 46]. The use of two alongside cuffed tubes (one tracheal 3.0 mm and one bronchial 3.5 mm) in a 11 kg child for unilateral WLL has been described [47]. Airway isolation has been obtained even for an infant as small as 2 kg [48]. When the perfect isolation of both lungs is obtained, WLL is performed similarly as when a DLT is placed but with much more attention to the stability of the airway devices.

When the techniques described above cannot be applied, mainly in patients weighing less than 10 kg, ECMO can be used to oxygenate the patient while bilateral simultaneous WLL is performed. Different approaches for the vascular

cannulation have been described [49, 50]. Finally, one case report described the use of partial liquid ventilation with perflubron (LiquidVent  ; Alliance Pharmaceuticals Corp. and Hoechst Marion Roussel) for 4 days following WLL done under ECMO in a 3.4 kg infant aged 6 weeks [51].

## Conclusion

After more than 50 years of evolution, whole lung lavage is an efficient and safe technique. This procedure can be adapted to a large variety of patients and diseases. When WLL does not lead to a substantial effect, there are now new modalities that can be combined to WLL.

## Clinical Case Discussion

A 47-year-old woman was referred to our team for WLL 10 years ago (2008). At that time, she presented some symptoms, mainly increasing dyspnea, for 6 months. An open lung biopsy had been performed at her hospital to establish the diagnosis of PAP. Pulmonary function tests performed in our center showed a light restrictive syndrome, a DLCO at 58%, and a PaO<sub>2</sub> of 68 mmHg. Radiological investigation revealed a homogeneous distribution with the involvement of bilateral superior lobes, middle lobe, and bilateral superodorsal segment of the inferior lobe. BAL confirmed the diagnosis of PAP.

A first bilateral WLL was performed, and moderately effective results were obtained. During the next 2.5-year period, the patient underwent six bilateral WLL, at intervals varying between 4 and 12 months, without good improvement in the clinical status, laboratory results, and radiological imaging. During the last WLL, BAL was performed as the radiological infiltrations were localized mainly in the left superior lobe and the supero-dorsal segment of the bilateral inferior lobes.

Nine months later, the patient complained about the same symptoms without marked improvement following any of the performed WLL. The dosage of GM-CSF was measured, and the dosage result, 203 µg/mL ( $N < 3$  µg/ml), confirmed the diagnosis of primary PAP. In the following months, the patient received GM-CSF, but this treatment was ended because no improvement occurred and many secondary effects were observed. A few months later, the patient was placed on rituximab (Rituxan ), but the treatment was also ended after a few cycles since there was clinical and radiological deterioration.

Given this situation, we performed a new WLL, associated with specific BAL. The sediment recuperation was increased following the BAL. In the following days after the

recovery from the WLL, we began GM-CSF by inhalation, once daily. At 1- and 3-month follow-up, the patient presented a significant improvement of her clinical status, for the first time since the first WLL. The radiologic images were completely cleared with this associated therapy, but the laboratory investigation remained stable.

We followed her to evaluate the long-term effect of this therapy. Up to 4 years after the last WLL, she received GM-CSF by inhalation following the yearly CT scan imaging, since the images reported small infiltrations. The last follow-up was done 8 years following the last WLL, and she was still asymptomatic. The annual CT scan was clean, as for the last four ones, and she did not take any GM-CSF inhalation.

This case report promotes the usefulness of a multimodal therapy that should be carried out to efficiently treat patients suffering from PAP.

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