nonhospice patients are very sensitive to how these types of patients are accounted for in the models.

Using expenditure data from a study (2) of the effect of hospice on expenditures in dying nursing home residents, we found that even in this more homogeneous sample a propensity score model similar to that used by Campbell and colleagues did little to control for selection bias compared with group-specific propensity score models incorporating a larger set of confounders. Underlying heterogeneity will be even larger if nursing home and non–nursing home populations are combined, as they were in Campbell and colleagues' study. The authors' use of propensity score by cohort with a modest list of confounders is unlikely to satisfactorily control for selection among such heterogeneous hospice samples. In addition, Campbell and colleagues' operational definition of low use may be confounded with hospice choice, biasing results toward no hospice effect (defined as a hospice-to-nonhospice expenditure ratio of 1) (compare ratios in Campbell and colleagues' Tables 2 and 3). Low use is less likely to differentiate patient preferences for aggressive care among the long-stay nursing home residents who contribute substantially to the increased cost associated with hospice (2).

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IN RESPONSE: The letter from Drs. Gozalo, Mor, and Miller appears to raise 2 issues. One concerns potential bias in our hospice effect estimation related to controlling for consistently low service use for 24 months before death. We did test for the effect of this variable and stated that the results persisted among all sensitivity analyses, including "models that do not correct for consistently low Medicare use."

The other issue turns on the effectiveness of propensity scores to control for selection bias, particularly in study samples, such as ours, in which nursing home residents are combined with community dwellers. Our analyses, including calculation of propensity score, were stratified by age group and condition cohort. Within each of these relatively homogeneous strata, models estimating hospice effects controlled not only for propensity score and for nursing home residence but also for an array of measures previously shown to correlate with hospice use: duration of illness, disease burden, gender, race, Medicaid enrollment, and urban or rural influences. Our discussion of limitations acknowledged that even if poststratification is used to match decedents by age and condition and propensity scores are used to control for other hospice selection effects, some selection bias will inevitably remain in an observational study design.

We sought methods that improved upon those applied in previous research concerning hospice effects on Medicare expenditures. We welcome future studies that offer additional methodologic improvements. Our study mainly shows that the quality and costs of various strategies to serve patients coming to the end of life deserve careful study.

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CLINICAL OBSERVATION

Editor's Note: The second author of the following Clinical Observation was one of a dozen Associates of the American College of Physicians selected to present a clinical vignette at the 2003 Annual Session in Philadelphia. We are proud to present this case report through a special arrangement with the Council of Associates of the College.

Silo-Filler's Disease, the Acute Respiratory Distress Syndrome, and Oxides of Nitrogen

TO THE EDITOR: *Background:* Oxides of nitrogen can both harm and help human health. For example, silo-filler disease is a form of acute lung injury caused by exposure to nitrogen dioxide (NO_2), but inhaled nitric oxide can improve oxygenation in patients with the acute respiratory distress syndrome (ARDS).

Objective: To describe a case of ARDS due to silo-filler's disease that was treated with inhaled nitric oxide, demonstrating how oxides of nitrogen can both harm and help human health.

Case Report: A 29-year-old male farmer was admitted to Fletcher Allen Health Care at The University of Vermont for management of respiratory failure. The patient had been in good health until 1 day before admission, when he opened the door to a corn silo and was engulfed in a yellow-orange gas that smelled like rotten eggs. He immediately developed severe dyspnea, lightheadedness, and diaphoresis. On presentation to the hospital he was hypoxemic, and chest radiographs showed bilateral pulmonary infiltrates. He was intubated and mechanically ventilated for respiratory support.

The patient was given a diagnosis of ARDS secondary to NO_2 inhalation from silo gas. He was maintained on mechanical ventilation using the low tidal volume, high positive end-expiratory pressure strategy, but he remained difficult to oxygenate. Despite inverse ratio ventilation, his oxygenation deteriorated and he required fluids and pressors for hemodynamic support. Steroids were administered for the possibility of bronchiolitis as a sequela of silo-filler's disease (1). As a last resort, inhaled nitric oxide was considered as therapy to improve oxygenation (2) and was subsequently started at 40 parts per million (ppm). Minutes after the inhaled nitric oxide was started, oxygen saturation increased by ten percentage points. Inhaled nitric oxide was continued at 20 ppm and was then gradually weaned over the next 3 days as the patient continued to improve. The remainder of his hospital course was uneventful, and he fully recovered.

Discussion: Silo-filler's disease is an acute lung injury caused by inhalation of toxic gases in or near an agricultural silo (1). Sudden death was first reported in a silo in 1914 (3). Unexplained deaths continued to be reported in the literature, with most toxicity wrongly attributed to carbon dioxide asphyxiation. It wasn't until the 1950s that NO_2 exposure in recently filled closed silos was implicated as the cause of silo-filler's disease (4). Despite this association, a new generation of farmers, among whom the use of open-bunker silos is more common, may be unaware of the potential risks involved with this potentially fatal but preventable disorder.

Although we were well aware of the seeming paradox of using inhaled nitric oxide to treat NO_2 toxicity, we treated our patient with inhaled nitric oxide as a last resort to improve his oxygenation. Inhaled nitric oxide is a pulmonary vasodilator that decreases pulmonary artery pressure and increases arterial oxygen tension in patients with ARDS (2). To date, studies on inhaled nitric oxide have demonstrated improved oxygenation but little hemodynamic effect and no significant improvement in mortality (2, 5). Methemoglobinemia may occur if a patient is exposed to both nitric oxide and NO_2; in this case, the maximum measured methemoglobin level was 0.9%.

We speculate that inhaled nitric oxide contributed to this patient's overall improvement by increasing his oxygenation and thereby improving his hemodynamic status. The damage done by the NO_2 had resolved, and the addition of a small amount of inhaled nitric oxide had only beneficial effects, without inducing further injury.

Conclusion: We believe that the temporal relationship of events in this case supports the view that inhaled nitric oxide changed our patient's clinical course. This case illustrates how oxides of nitrogen can be a double-edged sword.

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Email to a colleague

Silo Filler's Disease

Article Last Updated: Sep 6, 2006

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Author and Editor Disclosure

Synonyms and related keywords: silo unloader disease, nitrogen dioxide poisoning, SFD, silo-filler's disease, proliferative pulmonary disease, pulmonary edema, bronchiolitis obliterans, asphyxiation, methemoglobinemia, chemical pneumonitis, acute respiratory distress syndrome, ARDS, acute lung injury, nitrogen oxides, bronchioles lung injury, alveoli lung injury, arterial blood gas, ABG, methemoglobin, MHb, methemoglobinemia

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Background

Silo filler's disease (SFD) is an occupational disease that results from pulmonary exposure to oxides of nitrogen. SFD is a preventable occupational hazard that can be eliminated by proper work practices.

Nitrogen dioxide is a reddish brown gas that emits an odor similar to that of household bleach. It forms rapidly in farm silos that are filled with fresh organic material (eg, corn, grains). Hours after the organic material is stored, toxic and lethal levels of nitrogen dioxide, which is heavier than air, develop on top of the silage.

The clinical presentation of SFD depends on the duration of exposure and the concentration of this gas. Without proper precautions, farm workers entering a silo or remaining near the open hatches during the first 10 days after filling may experience various degrees of exposure. Most symptomatic exposures are mild and self-limiting; however, some events may cause sudden death from asphyxiation, pulmonary edema, or, weeks later, bronchiolitis obliterans. Low concentrations of nitrogen dioxide may cause cough, dyspnea, fatigue, upper airway irritation, and ocular irritation. With an increase in concentration and duration, the individual may experience cyanosis, vomiting, vertigo, and a loss of consciousness. More severe exposure can result in acute respiratory distress syndrome (ARDS), laryngeal spasm, bronchiolar spasm, reflex respiratory arrest, or asphyxia.

The first recorded incidence of a death from SFD was in 1914 when 3 men fell into a silo and were asphyxiated by an unknown gas (ie, unknown at that time). The term silo filler's disease was coined in 1956.

Pathophysiology

In the lung, nitrogen dioxide hydrolyzes to nitrous and nitric acid, causing profound chemical pneumonitis and pulmonary edema. Nitrogen dioxide hydrolyzes slower than some water-soluble gases, resulting in deep lung injury in the bronchioles and alveoli. Type I pneumocytes and ciliated airway cells are primarily affected, but damage also occurs from free radical generation, which results in protein oxidation, lipid peroxidation, and cell membrane damage. Nitrogen oxides can alter immune function and macrophage activity, leading to an impaired resistance to infection. Additionally, high levels of carbon dioxide in the silo may stimulate a deeper inspiration of the gases, causing a higher delivered dose.

Significant exposure can also result in methemoglobinemia. Nitrogen dioxide binds to hemoglobin with a great affinity, forming nitrosyl hemoglobin, which is readily oxidized to methemoglobin. Methemoglobin results in a leftward shift of the oxygen disassociation curve, which impairs the oxygen delivery and compounds the already present hypoxia.

Frequency

United States

SFD is prevalent during the harvest months of September and October. During other months, consider other etiologies first. An estimated annual incidence of 5 cases per 100,000 silo-associated farm workers per year was reported in New York. SFD is likely significantly underreported.

Mortality/Morbidity

Exposure is usually mild and self-limiting; however, some exposure results in pulmonary edema, bronchiolitis obliterans, or rapid asphyxiation. In one study, approximately one third of people with severe exposures died from pulmonary edema and bronchiolitis obliterans.

- Sudden death and asphyxiation: Death can result from bronchiolar spasm, laryngeal spasm, reflex respiratory arrest, or asphyxia. Nitrogen dioxide concentrations can be sufficiently high, causing displaced oxygen, complete asphyxiation, and death. High concentrations can render a person helpless within 2-3 minutes.

- Pulmonary edema: The chemical irritation of the alveoli and bronchioles results in rapid destruction of the epithelial cells generating fluid accumulation in the lung tissue by breakdown of the pulmonary capillary bed.

- Bronchiolitis obliterans: Failure to treat SFD with corticosteroids can result in the development of fibrous granulation tissue within small airways and alveolar ducts, occurring weeks or months after the initial incident. This results in a permanent restrictive lung disease.

Race

No epidemiologic studies indicate a racial predilection.

Sex

SFD is an agricultural occupational disease, and it historically has predominantly affected the male farm worker; however, gender is unlikely to play a role in the pathophysiologic response.

Age

Adults are at highest risk to develop SFD; however, nitrogen dioxide exposure can also affect children and livestock near a fresh silage pile.

History

- Occupational medical history
  - Obtain a complete occupational medical history and be familiar with the pattern of disease caused by nitrogen dioxide.
  - If the patient presents immediately postexposure, the full injury may not be appreciated; effects may occur up to 24 hours after the event.
  - September and October (ie, harvest season) are the primary months that silo filler's disease (SFD) occurs and should influence diagnostic decision-making.
- Acute symptoms
  - Common symptoms are coughing, light-headedness, dyspnea, tightness in the chest, choking, diaphoresis, and loss of consciousness.
  - Coughing is the most common symptom; however, it may not occur in all patients.
  - Wheezing, chest pain, weakness, throat and ocular irritation, and nausea are less common symptoms.
  - Nitrogen dioxide is not as soluble as other gases (eg, chlorine); consequently, mucous membrane irritation is not common.
- Persistent or delayed symptoms - May appear days or even weeks later
  - Symptoms include dyspnea, coughing, chest pain, rapid breathing, tightness in the chest, headache, and fever.
  - Less frequent symptoms include insomnia, wheezing, chills, light-headedness, myalgias, nausea, hemoptysis, palpitations, and blue lips.
  - Some cases of SFD resolve with no persistent or delayed symptoms.

Physical

The findings on physical examination may appear normal initially, but findings often include the following:

- Decreased breath sounds
- Rales
- Rhonchi
- Wheezing
- Conjunctival injection

- Cyanosis (caused by the presence of methemoglobin and impaired pulmonary gas exchange)
- Hemoptysis
- Unresponsiveness
- Systemic hypotension
  - Nitric oxide formation generates vasodilation and reduced systemic vascular resistance resulting in hypotension.

Causes

- Silos filled with freshly cut corn, oats, grass, alfalfa, or other plant material generate oxides of nitrogen within hours. Maximum concentrations of nitrogen dioxide are reached within 1-2 days, and then the levels begin to fall after 10-14 days. In well-sealed silos, nitrogen dioxide can be present for weeks. Silage that is heavily fertilized, has experienced drought, or is derived from immature plants results in much higher concentrations of nitrogen oxides within the silo.
- During storage, nitrogen dioxide, which is 1.5 times heavier than air, can remain in deep depressions of the silage material. Exposure can develop while attempting to level the silage without proper ventilation or breathing apparatus. One documented case occurred in an individual who traversed the ladder at the opening of a silo. The heavier-than-air nitrogen dioxide flowed down the side of the silo, exposing the worker to toxic levels of gas.

Acute Respiratory Distress Syndrome
Angina Pectoris
Anxiety Disorders
Chronic Obstructive Pulmonary Disease
Emphysema
Farmer's Lung
Hantavirus Pulmonary Syndrome
Metastatic Cancer, Unknown Primary Site
Methemoglobinemia
Miliary Tuberculosis
Myocardial Infarction
Myocardial Ischemia
Pneumonia, Aspiration
Pneumonia, Bacterial
Pneumonia, Fungal
Pneumonia, Viral
Pulmonary Edema, Cardiogenic
Pulmonary Embolism
Toxicity, Cyanide
Toxicity, Organophosphate
Toxicity, Salicylate

Other Problems to be Considered

Acute lung injury
Pneumonitis, other chemical
Pneumoconiosis
Conjunctivitis
Smoke inhalation
Toxicity, carbon monoxide
Toxicity, chlorine gas
Toxicity, hydrogen sulfide
Toxicity, carbamate
Toxicity, phosgene
Toxicity, ozone
Toxic organic dust syndrome

Lab Studies

- Silo filler's disease (SFD) cannot be diagnosed using any laboratory studies; however, the following studies can be helpful in excluding other causes of the symptoms.
- Arterial blood gas level
  - Measuring arterial blood gas (ABG) levels establishes the presence and severity of gas exchange impairment. Initial blood gas levels are extremely important in the decision to intubate.
  - Some available literature supports obtaining serial ABG levels during follow-up visits to ascertain whether bronchiolitis obliterans is developing.
- Lactate level: Metabolic acidosis can occur by dissolution of nitrous oxide in body fluids, resulting in tissue hypoxemia and subsequent lactic acid formation.
- Methemoglobin level
  - Perform a methemoglobin (MHb) test to evaluate cyanosis that does not respond to oxygen administration. MHb is an inactive oxidized form of hemoglobin that does not contribute to oxygen transport. Cyanosis results from an MHb test result that is greater than 10-15%.
  - Methylene blue administration can affect this test result.
- Complete blood count: Leukocytosis is often present in SFD.

Imaging Studies

- Chest radiography
  - Findings may be normal.
  - During acute injury, the chest radiograph shows ill-defined, alveolar opacities, which are characteristic of pulmonary edema or ARDS.
  - Subacute injury reveals small opacities or confluent woolly opacities. The small opacities can be mistaken for miliary tuberculosis.

Other Tests

- Pulmonary function test
  - As soon as the patient is able to undergo tests, conduct a pulmonary function test (PFT) to chart the progress and document the severity of disease.
  - A baseline PFT is helpful as the patient recovers.
  - Conduct PFTs at regular intervals toward the end of the inpatient stay and during follow-up visits.
- ECG
  - Symptoms of SFD can mimic cardiovascular events; ECG may help rule out such occurrences.
  - Serial ECGs are helpful for baseline and initial encounters; however, only abnormal findings are helpful.
- Pulse oximetry monitoring: Pulse oximetry monitoring may be misleading in the presence of methemoglobinemia.

- Pulmonary artery catheter: In patients who are critically ill, monitoring of mixed venous oxygenation and pulmonary vascular resistance may assist in the management of oxygenation requirements, fluids, ARDS, and physiologic variables.

Procedures

- Intubation and mechanical ventilation may be necessary if gas exchange is severely impaired.

Histologic Findings

In patients who quickly die, hemorrhagic edema and patches of pneumonia are revealed in their airways. Small palpable nodules and hemorrhagic areas appear in those patients who survive for several weeks.

Microscopic evaluation of tissues from patients with acute SFD shows edema and extensive damage of the respiratory epithelium, which may be completely shed in the small bronchi and bronchioles. In patients who survive for longer periods, generalized infiltration of the alveolar walls with lymphocytes (ie, numerous macrophages in alveolar spaces) occurs. Bronchiolitis obliterans occurs in various stages of organization and is responsible for the palpable nodules.

Medical Care

- Prehospital care: Safely remove the patient from exposure without endangering rescuers.
- Medical care
  - Hospitalize the patient for 12-24 hours for observation or longer if gas exchange is compromised.
  - Administer oxygen to the patient for hypoxemia.
  - Use mechanical ventilatory support for hypoxemic or hypercapnic respiratory failure. Treat secondary infection, if present.
  - Administer volume expanders cautiously.
  - The patient may require invasive monitoring because excessive administration of volume expanders can cause hydrostatic pulmonary edema. Nitrogen dioxide forms nitric oxide, causing vasodilation and an apparent volume depletion.
  - Monitor continuous pulse oximetry.

Consultations

- Consult a pulmonary medicine or critical care specialist if the patient requires endotracheal intubation or hemodynamic monitoring.
- Consult a medical toxicologist or poison control center to provide additional information and patient care guidelines.

Activity

Advise the patient to avoid exercise for 1-2 days after exposure.

MEDICATION

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Methylene blue is indicated for significant methemoglobinemia. Other possible treatments may include antibiotics if infection becomes evident, and vasopressor drugs are required to correct the normovolemic shock. Corticosteroids may be important in the prevention of bronchiolitis obliterans.

Drug Category: *Antidotes*

Methylene blue (ie, tetramethyl thionine chloride) is the recommended antidote for methemoglobinemia. It is reduced to leukomethylene blue, which is then available to reduce methemoglobin to hemoglobin.

Drug Name	Methylene blue (Urolene Blue)
Description	Used if methemoglobin exceeds 30%. Administer IV.
Adult Dose	1-2 mg/kg IV over 5 min at 1% solution; repeat dosing in 1 h if continued symptomatology or significant methemoglobinemia is present; not to exceed 7 mg/kg
Pediatric Dose	Administer as in adults; 0.3-1.0 mg/kg IV over 5 min for neonates
Contraindications	Documented hypersensitivity; intraspinal administration; severe renal insufficiency; treatment of methemoglobinemia in cyanide poisoning
Interactions	None reported
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	High doses (5-10 mg/kg) or rapid IV administration may induce acute hemolytic anemia or cause further methemoglobin production; patients with a glucose-6-phosphate deficiency may not benefit from this treatment; toxic effects include dyspnea, precordial pain, restlessness, apprehension, a sense of oppression, and tremors

Drug Category: *Corticosteroids*

These agents do not benefit the patient during the acute phase, but they are effective in treating bronchiolitis obliterans. Because not all patients with acute lung injury develop bronchiolitis, judge the risk factors and choose between prescribing the patient corticosteroids as prevention and monitoring the patient for clinical or radiographic evidence of bronchiolitis obliterans.

Drug Name	Methylprednisolone (Adlone, Solu-Medrol, Depo-Medrol)
Description	Reduces inflammatory response of bronchiolitis obliterans and can be tapered over 8 wk, adjusting the dose based on clinical symptoms, radiographs, and spirometry.
Adult Dose	125 mg IV q6h initially; follow with 40 mg/d PO, tapering to 20 mg/d over the first mo, then gradually wean off over the next mo
Pediatric Dose	Not to exceed 30 mg/kg IV

Contraindications	Documented hypersensitivity
Interactions	Coadministration with digoxin may increase digitalis toxicity secondary to hypokalemia; estrogens may increase levels of methylprednisolone; phenobarbital, phenytoin, and rifampin may decrease levels of methylprednisolone (adjust dose); monitor patients for hypokalemia when taking medication concurrently with diuretics
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Hyperglycemia, edema, osteonecrosis, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, growth suppression, myopathy, and infections are possible complications of glucocorticoid use

Drug Category: ***Inhalational agents***

One case report described a patient with ARDS secondary to SFD who required nitric oxide (NO) therapy because of worsening oxygenation. Great care should be instituted with nitric oxide therapy because of the possibility of worsening pulmonary damage and methemoglobinemia, which are already present in SFD.

Drug Name	Nitric oxide (INOmax)
Description	Produced endogenously from action of enzyme NO synthetase on arginine; relaxes vascular smooth muscle by binding to heme moiety of cytosolic guanylate cyclase, activating guanylate cyclase and increasing intracellular levels of cGMP, which then leads to vasodilation; when inhaled, NO decreases pulmonary vascular resistance and improves lung blood flow.
Adult Dose	20 ppm via respirator initially; not to exceed 80 ppm; effect of pulmonary vasodilatation may still be observed at 5 ppm; deliver by system that measures concentrations of NO in breathing gas with constant concentration throughout respiratory cycle; deliver by system that does not cause generation of excessive inhaled nitrogen dioxide
Pediatric Dose	20 ppm via respirator initially; not to exceed 80 ppm; most children respond at 20 ppm and can be weaned to lower doses; effect of pulmonary vasodilatation may still be observed at 5 ppm; deliver by system that measures concentrations of NO in breathing gas with constant concentration throughout respiratory cycle; deliver by system that does not cause generation of excessive inhaled nitrogen dioxide
Contraindications	Right to left shunting of blood; methemoglobin reductase deficiency
Interactions	Concomitant administration with NO donor compounds (eg, nitroprusside, nitroglycerin) may have additive effects and may increase risk of methemoglobinemia
Pregnancy	C - Safety for use during pregnancy has not been established.
Precautions	Abrupt discontinuation of NO may lead to worsening oxygenation and increasing PAP; toxic effects include methemoglobinemia and pulmonary inflammation resulting from reactive nitrogen intermediates; caution in thrombocytopenia, anemia, leukopenia, or bleeding disorders; monitor for PaO_2, methemoglobin, and NO_2; abrupt withdrawal causes rebound pulmonary hypertension

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FOLLOW-UP

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Further Inpatient Care

- Admit the patient for at least 24 hours if signs of dyspnea, altered mental status, hypoxemia, or a widened alveolar-arterial

oxygen gradient are present.

- If no initial symptoms are present, observe the patient for at least 12 hours for hypoxemia.
- Pulmonary edema can take up to 48 hours to develop. Educate the patient on the possible symptoms and instruct the patient to return if the symptoms develop.
- Clinical improvement and resolution of hypoxemia and methemoglobinemia are helpful endpoints for discharge.

Further Outpatient Care

- Conduct a follow-up examination at 1 week, 1 month, and 3 months after exposure, with serial PFTs and radiographs.

In/Out Patient Meds

- When the patient is discharged, prescribe corticosteroid taper for at least 8 weeks. A longer duration (ie, 6-12 mo) may be indicated if symptoms of bronchiolitis obliterans persist or recur after initial steroid taper.
- Inhaled sympathomimetics (eg, albuterol), anticholinergics (eg, ipratropium bromide), and steroids (eg, fluticasone propionate) may also be indicated if the patient has additional symptoms of reactive airway disease. A typical asthma disease management plan can be used for these patients.

Transfer

- Transferring the patient to a tertiary care center for further diagnostic evaluation and ventilatory support may be necessary.

Deterrence/Prevention

- Educate farm workers at risk for exposure.

Complications

- Secondary infection: Infection (eg, pneumonia) is possible because of the mucosal injury caused by pulmonary edema and the inhibition of immune function by nitrogen dioxide.
- Bronchiolitis obliterans: Fibrous granulation tissue develops within small airways and alveolar ducts, occurring weeks or months after the initial incident.

Prognosis

- Pulmonary function may not improve (without permanent disability) for weeks or months; however, mild dysfunction likely due to bronchiolitis obliterans may occur. This manifests as mild hyperinflation; abnormal V_{max50}, V_{max75}, or FEF_{25-75}; increased respiratory resistance; and airway obstruction.
- The lungs clear quickly with steroid treatment, and the chest radiograph may reveal no evidence of residual lung damage.
- Treat deconditioning by referring the patient to a pulmonary rehabilitation program.

Patient Education

- Offer the following preventive advice to the patient:
  - Stay out of the silos during the 2-week danger period after the initial filling.
  - Close all doors before putting in the silage.
  - Go up the outside ladder to the level of silage.

- If the silo is not completely full, remove the doors that lead down to the silage.
- Enter the silo only with a complete oxygen support system (ie, air supply, self-contained breathing apparatus).
- Ventilate the silo by opening the cover flaps and running the silo blower for 24-48 hours before entering.
- Never enter the silo alone or without a lifeline for rescue during the danger period.
- If entering a silo during filling is necessary, enter immediately after the last load.

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MISCELLANEOUS

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Medical/Legal Pitfalls

- Failure to inform the patient about delayed symptoms, including life-threatening pulmonary edema and dyspnea due to bronchiolitis obliterans
- Failure to consider the asymptomatic period and the delayed onset of symptoms associated with nitrogen dioxide toxicity
- Discharging the patient too soon from the emergency department
- Failure to consider nitrogen dioxide toxicity in patients who present with dyspnea and who have occupations allowing exposure
- Failure to recognize early signs of significant respiratory distress and to document either a PO_2, an Aa gradient, or oxygen saturation via pulse oximetry
- Failure to monitor the patient in a setting where respiratory support is immediately available
- Failure to monitor the patient for bronchiolitis obliterans or to prescribe the patient steroids when signs manifest

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