Oxygen Use: Recommendations For All Practice Settings

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By
Larry Cahalin, PT, PhD, CCS
Rohini Chandrashekar, PT, CCS
Rebecca Crouch, PT, DPT, CCS
Ann Fick, PT, DPT, CCS
Ellen Hillegass, PT, PhD, CCS
Susan Butler McNamara, PT, MMSc, CCS
Amy Pawlik, PT, DPT, CCS
Christiane Perme, PT, CCS

Overview of Presentation

• Introduction & Overview of Evidence
• Current Guidelines & Legal Issues of O2 Use
• Basics of O2 Delivery
  — Pulse Oximetry
  — O2 Delivery Devices
• Basics of O2 Use and Titration Of Oxygen
• O2 use in Acute Care
• O2 use in COPD and with CO2 retention
• O2 use in Cystic Fibrosis and Heart Failure
• O2 use in Interstitial Lung Disease (ILD) and Pulmonary Arterial Hypertension (PAH)
• Summary of Recommendations

Objectives

• Discuss current evidence of use of oxygen in practice including benefits, precautions and populations that benefit from use of oxygen.
• Discuss legal issues with use of oxygen including any limitations in state practice acts.
• Define and differentiate the modes of delivery of oxygen as well as use of pulse oximetry
• Discuss indications and contraindications for titration of oxygen and populations that should be used with caution.
• Identify practical tips with the use of oxygen in the clinic or when patients travel.
• Discuss indications for use as well as the similarities and differences of oxygen use for all populations seen by PTs and PTAs.
• Summarize recommendations of O2 use in all clinical settings based upon current evidence and provide suggestions for further research

Why a Task Force on O2 Recommendations?

• Therapists from every practice setting and every state ask CV & P section for information and help on this issue
• Lack of knowledge of evidence on O2 use in all populations
• PTs fear legal issues on all aspects of O2 use, especially titration as well as fear with O2 use in COPD and CO2 retainers
• Lack of knowledge of evidence and guidelines
• Need exists for PTs to have recommendations for their profession

Hypoxemia: What is It?

• Hypoxemia is defined as a decreased partial pressure of Oxygen (PaO2) less than 60 mm Hg or with an SpO2< 90%
• Normal ABG values:
  — pH 7.35-7.45
  — pCO2 35 – 45 mm Hg
  — PO2 80 – 100 mm Hg
  — HCO3 22-26
• As PaO2 decreases, SpO2 decreases

Hypoxemia: Causes & Examples

• Causes of Decreased PaO2 include:
  — Alveolar hypoventilation
    • Clinical example: atelectasis secondary to post op thoracic or abdominal pain
  — Decreased ventilation (either decreased volume or decreased rate)
    • Clinical example: decreased volume – inability to breathe in adequate volume due to pleural effusion or pulmonary edema
    • Clinical example: decreased rate – sedated or comatose causing decreased respiratory rate
Hypoxemia: Causes and Examples

- Ventilation perfusion mismatching
  - Clinical example: Pulmonary embolus or patient with poor cardiac output
- Low inspired partial pressure of oxygen
  - Clinical example: high altitude
- Impaired diffusion across alveolar-capillary membrane
  - Clinical example: interstitial edema, pulmonary fibrosis impairing diffusion across alveolar wall
- Shunting
  - Clinical example: Pulmonary embolus, emphysema

Hypoxemia: Examples

- Ventilation perfusion mismatching
- Low inspired partial pressure of oxygen
- Impaired diffusion across alveolar-capillary membrane
- Shunting

Hypoxemia: Consequences

- Hypoxemia has several physiologic consequences:
  - As PaO₂ falls below 55 mm Hg; marked rise in VE (Minute ventilation) with fall in PaCO₂
  - Peripheral vascular beds dilate causing compensatory HR rise (tachycardia) and Cardiac Output increase to increase O₂ delivery
  - Regional pulmonary vasoconstriction occurs due to alveolar hypoxia
  - Erythropoietin secretion increases: increase in erythrocytosis and increase in O₂ carrying capacity

Hypoxemia: Long term effects

- Polycythemia
- Pulmonary hypertension
- Right ventricular failure (cor pulmonale)
- Chronic hypoxemia with cor pulmonale results in poor prognosis: increased mortality (32-100%) *
- Cellular changes:
  - Mitochondrial function declines
  - Anaerobic glycolysis occurs
  - Lactate/pyruvate ratio increases

* Jones 1967, Boushy 1973

Hypoxemia: Long term Clinical Manifestations

- Impaired judgment at low levels of hypoxemia
- Progressive loss of cognitive and motor functions
- Loss of consciousness with severe hypoxemia
- Other
  - Headache
  - Breathlessness/ severe dyspnea
  - Palpitations
  - Angina
  - Restlessness
  - Tremor

Manning 1995, Lane 1987, Criner & Celli 1987

Short Term Effects of O₂

- Improves breathlessness with exercise in COPD patients
- Improves exercise tolerance in those with mild, moderate or severe hypoxemia w/exercise
- Proposed Mechanisms:
  - Decreased VE (Swinburn 1991 Am Rev Resp Dis)
  - Decrease in dynamic hyperinflation (O’Donnell 2001)
  - Alleviation of hypoxic pulmonary vasoconstriction (Dean 1992)
  - Improvement in hemodynamics (Dec PVR, Inc CO) (Dean 1992)
  - Increase in O₂ delivery (Morrison 1992)
  - Improvement in ventilatory muscle function (Bye 1985)
  - Altered ventilatory muscle recruitment (Criner & Celli 1987)
  - Reflexive inhibition of central ventilatory drive ( Manning 1995)
  - Decreased perception of dyspnea (Lane 1987)
What are Indications for Short Term Oxygen Therapy?

- $\text{PaO}_2 < 55 \text{ mm Hg or SpO}_2 < 88\%$
- $\text{PaO}_2 \geq 55 \text{ mm Hg but } \leq 59 \text{ mm Hg and additional diagnoses (PAH, cor pulmonale)}$
- $\text{PaO}_2 \geq 60 \text{ mm Hg or SpO}_2 \geq 90\% \text{ but patient desaturates during activity: should use short term O2 with all activities}$

Kim 2008 Proc Am Thor Soc

Effect of LTOT

- Early non-controlled studies:
  - Reduction in mortality in COPD, cor pulmonale and those with severe hypoxemia with use of continuous O2 7-41 mos.
- Two landmark prospective controlled studies
    - Continuous O2 versus 12 hrs Nocturnal O2
    - Mortality was > for nocturnal O2 vs. continuous O2
  - British Medical Research Council (MRC) Long Term Domiciliary O2 Therapy Trial (Lancet 1981)
    - Trend that LTOT prevented progressive decrease in PO2 and increase in pulm vascular resistance without increase in PCO2

LTOT

Conclusions from 2 studies (population was severely hypoxemic with elevated HCT, elevated PA pressure and Respiratory acidosis
- Nocturnal O2 is better than NO oxygen therapy
- Continuous O2 better than nocturnal O2 therapy
  - No studies have shown benefit with mild or moderate hypoxemia
  - No studies have shown benefit when O2 prescribed for exercise-induced O2 desaturation

Indications for Long-Term O2 Therapy

Kim 2008 Proc Am Thor Soc

Current O2 Guidelines

- Clinical Practice Guidelines Oxygen Therapy for Adults in the Acute Care Facility—2002 Revision and Update AARC
- Australian and New Zealand Guidelines for management of COPD 2009 (Abramson; AM Lung Assn 2009)

Legal Issues with O2 Use

- APTA Legislative Department knows of no state that has any limitations on Physical Therapists in use of or titration of Oxygen
- Oxygen is a DRUG and requires a prescription for its use.
- Oxygen order should be written based upon SpO2 and not Liters/minute.
  - Always check standing orders or patient’s specific orders
  - Desire order to be written: Keep SpO2 ≥ 90 or 88%
  - Order may be written 2L/min OR SpO2 ≥ 90 or 88%
- One State: Connecticut has new changes in their law for use of O2 in hospitals
PT State Practice Acts

• Physical therapy practice acts and physical therapy board regulations are SILENT on the administration of oxygen. However, some state/jurisdiction licensing authorities have provided official interpretive opinions/statements on this issue. Check with your state/jurisdiction licensing authority to determine if your state board has an official statement or opinion regarding the administration of oxygen. To contact your state licensing board, follow this link: http://www.fsbpt.org/licensing/index.asp.

APTA Position Statement

• PHARMACOLOGY IN PHYSICAL THERAPIST PRACTICE HOD P06-04-14-14 (Program 32) [Initial HOD 06-89-43-89]

  • [Medications in the Provision of Physical Therapy] [Position]
  Physical therapist patient/client management integrates an understanding of a patient’s/client’s prescription and nonprescription medication regimen with consideration of its impact upon health, impairments, functional limitations, and disabilities.

  • The administration and storage of medications used for physical therapy interventions is also a component of patient/client management and thus within the scope of physical therapist practice.

  • Physical therapy interventions that may require the concomitant use of medications include, but are not limited to, agents that:
    • Promote integumentary repair and/or protection
    • Facilitate airway clearance and/or ventilation and respiration
    • Facilitate adequate circulation and/or metabolism
    • Facilitate functional movement.

Guide to Physical Therapist Practice

• APPENDIX 1: Guide to Physical Therapist Practice

  – Prescription, Application, and as Appropriate, Fabrication of Devices and Equipment
  Interventions
  Prescription, application, and, as appropriate, fabrication of devices and equipment may include:
  • Supplemental Oxygen

Connecticut Law

• Sec. 80. (NEW) (Effective October 1, 2010) A hospital, as defined in section 19a-490b of the general statutes, may designate any licensed health care provider and any certified ultrasound or nuclear medicine technician to perform the following oxygen-related patient care activities in a hospital:
  • (1) Connecting or disconnecting oxygen supply;
  • (2) transporting a portable oxygen source;
  • (3) connecting, disconnecting or adjusting the mask, tubes and other patient oxygen delivery apparatus; and
  • (4) adjusting the rate or flow of oxygen consistent with a medical order.

  Such provider or technician may perform such activities only to the extent permitted by hospital policies and procedures, including bylaws, rules and regulations applicable to the medical staff. A hospital shall document that each person designated to perform oxygen-related patient care activities has been properly trained, either through such person’s professional education or through training provided by the hospital. In addition, a hospital shall require that such person satisfy annual competency testing. The provisions of this section shall not apply to any type of ventilator, continuous positive airway pressure or bi-level positive airway pressure units or any other noninvasive positive pressure ventilation.

Basics of O2 Delivery: Measurement and Devices

Pulse Oximetry

O2 Delivery Devices
Pulse Oximetry
Ann Fick PT, DPT, MS, CCS

Pulse Oximeter

• Pulse oximeter:
  – Can be used continuously to help provide clinicians with insight into a patient’s oxygenation status at rest as well as during activity
  – Noninvasive and cost-effective method of measuring a patient’s heart rate & the percentage of blood (hemoglobin) saturated with oxygen

Pulse Oximeter

• How does it work?
  – Attached to the computerized device is a probe with a light emitter and a photodetector aligned directly opposite and facing each other.
  – The light emitter produces a red and an infrared light which is absorbed by the hemoglobin in the blood.
  – The photodetector portion of the probe measures this light in order for the machine to generate an estimated oxygen saturation value.

Pulse Oximeter

• What does it actually measure?
  – The percentage of hemoglobin saturated with oxygen
  – Hemoglobin-protein within the red blood cells responsible for transporting oxygen to the tissues
  – Each molecule has 4 sites that can bind with oxygen
  – If a patient is anemic, there is less hemoglobin to carry O₂ to the heart and other cells. All of the hemoglobin molecules may be fully saturated with O₂ i.e. 100% but there still may not be enough O₂ for the needs of the body.

Pulse Oximeter

• Normal acceptable SpO₂ values range from 95 to 100%
• Lower values often seen in people with pulmonary and some cardiac disease processes
• American Thoracic Society suggests oxygen supplementation for patients for:
  – SpO₂ of ≤88%
  – SpO₂ ≤ 89% in special situations e.g. pulmonary hypertension & cor pulmonale

Pulse Oximeter

• Physical Therapists frequently conduct 6 MWT & provide interventions for individuals with cardiovascular and pulmonary as well as other patients exhibiting low SpO₂ values.
• Values are critical for us to assess in order to help determine a patient’s oxygen needs at rest & with activity
• Important to note -pulse oximetry is only a tool and needs to be utilized correctly
• We must be aware inaccurate readings can occur. Therefore, it is important to recognize and minimize limitations that hinder accuracy of pulse oximeters.
Pulse Oximetry Errors

• Multiple factors can hinder the accuracy of pulse oximeter readings including:
  – Motion and weight bearing which can produce extra “noise” that interferes with the signal transmitted to the machine
  – Placement of the probe
    • 3rd and 4th fingers have been shown to produce more accurate readings than the index finger
    • Finger probe placement usually more accurate than earlobe probe placement
    • Use a forehead probe if finger and ear probes are inaccurate

Pulse Oximetry Errors

• Dirt, fingernail polish or anything blocking sensor light path
  – The machine is calibrated to account for the tissue & bone of the finger when using a finger probe
  – It is also calibrated to account for the tissue/cartilage in the ear when using an ear probe
  – But, it assumes nothing else, e.g. dirt, is blocking the light passing from the emitter to the detector.

Pulse Oximetry Errors

• Incorrect probe size, wrong probe type
  – Use pediatric size probes for children and adult size probes for adults
  – Use the ear probe on the ear and the finger probe on the finger
  – The machine uses a predetermined path length from the emitter to the detector for each situation therefore the distance is obviously different for children vs. adults and for the finger vs. the ear
    • (For example…..If you put an ear probe for an adult on the finger of an adult. In this case, the machine assumes the path length should be much shorter than it actually is for the finger AND it assumes the light needs to go through cartilage only, not a fingernail and bone also.)

Pulse Oximetry Errors

• Low Perfusion/Dysrhythmias
  – Good perfusion is needed for a machine to read the signal correctly. In patients with poor perfusion (or some heart beats with lower perfusion e.g. atrial fibrillation), the machine has difficulty distinguishing this weak signal from any “noise” 2nd to patient movement etc.

• “Probe off” false reading
  – Probe is actually off of the finger or ear but a value is given by the machine 2nd to i.e. excessive ambient light

Pulse Oximetry Errors

• Incorrectly positioned sensor
  – If the emitter and detector sensors (esp. of a disposable probe) are not in proper alignment, false low readings of oxygen saturation on all pulse oximeters occurs. When light is shunted around the finger vs. through the finger, it appears that very little light is absorbed by the hemoglobin in blood.

Pulse Oximetry Errors

• Machine maintenance:
  – Clean machine/cable/probe with minimum amount of alcohol since harsher chemicals can cause corrosion or damage to the unit
  – If a bleach solution must be used, clean the machine with a slightly wet cloth (water only) in order to minimize corrosion
  – Put the monitor in a clear glove or Ziploc bag for use in isolation areas for protection
  – Use boot since this rubberized material helps minimize any shock to machine if dropped
  – Wrapping cable wires around the machine eventually causes the wires to break and cable will quit working
Clinical Notes When Using a Pulse Oximeter

- Many factors can influence a patient’s SpO₂ value on the machine such as:
  - Anemia
  - Low perfusion
  - Errors such as using the wrong probe type or noise interference such as motion
- Therefore, be sure to compare the actual heart rate with the heart rate given by the machine to assure accuracy of the machine

Clinical Notes When Using a Pulse Oximeter

- Proper documentation is crucial
  - Note vitals as well as signs/symptoms the patient exhibits relating to hypoxemia
- No pulse oximeter is a substitute for good quality clinical assessment of the patient’s status

Oropharyngeal Airway

- Purpose:
  - Keeps the tongue away from the back of the throat
  - Facilitates suctioning of airway
- Other:
  - A common obstruction in an unconscious pt is the tongue
  - This places the tongue in the proper position and makes it easier for the pt to breathe

Oxigen Delivery Systems

Rebecca Crouch, PT, DPT, CCS

Oxygen Delivery Systems

- Low flow – more variable performance
- High flow – more fixed performance
- Formula for hospital type E cylinders for amount of time left in tank
  - \( \text{pounds/square inch} \times k \)
  - Desired flow rate
  - \( k = 0.28 \) for E cylinder
  - Psi – read off regulator dial
FiO₂

- The fraction of inspired oxygen
- % of inhaled air that is oxygen
- Room air =21% O₂
- Document FiO₂ when patient using Venturi and Face Mask/Trach collar (not flow rate or L/min)

Pulse Oximeter

Nasal Cannula (NC)

- Low-flow O₂ system
- Increases O₂ concentration pt. breathes in
- Range of O₂ concentration is ~ 24% to 44%

O₂ Concentrations of Patients Using a Nasal Cannula

- Normal given ranges of O₂% with NC:
  - 1 L/min  24%
  - 2 L/min  28%
  - 3 L/min  32%
  - 4 L/min  36%
  - 5 L/min  40%
  - 6 L/min  44%

High Flow Nasal Cannula

- Best for patients needing more than 6 L/min NC
- Highest % O₂ is up to 75% FiO₂ at 15 L/min
- New to many clinics
- More comfortable, can eat/drink/talk easier than with mask
Oxymizer

• Specialized NC with O2 reservoir that conserves O2
• Uses 25-75% less O2 (the less O2 needed by the patient, the higher savings of O2)
• Therefore a good way to deliver O2 at home

Comparison of O₂ Concentrations During Oral and Nasal Breathing With Nasal Cannula

• FiO₂ is actually somewhat variable per liter
• There is a significant difference of FiO₂ that patients attain during oral and nasal breathing at rest
• Mouth breathers get a higher FiO₂ (NC mouth)
• During hyperventilation, FiO₂ of oral and nasal breathers will probably decrease

Face Mask

• O₂ system that increases O₂ concentration to the range of 35-55%
• To determine the FiO₂ the pt is receiving, check the “dial” (nebulizer cap) on the bottle attached to the wall O₂. The flow of the O₂ from the wall O₂ tank stays at 8-10 L/min.
• If the flow is at i.e. 5 L/min or less, then exhaled air may be re-breathed by pt
Venturi System

• O₂ system that provides a more specific O₂ concentration to the pt than other devices
• When the size of the orifice and O₂ flow increase, the pt receives an increased % of O₂. The other opening allows room air to be added
• FiO₂ from Venturi is 24-50%
• It is an easy system to use to ambulate pts

Partial Non-rebreather Mask

• Mask with an O₂ reservoir (bag) that provides a higher amount of O₂ to patient
• NRB flow
  - 6L/min = 60%
  - 7L/min = 70%
  - 8-10L/min = 80+
• Advantage – requires a lower flow of O₂ for the FiO₂ needed

Endotracheal Tube & Ventilator

• Purpose:
  – Aid in breathing/protecting the airway when a patient is on the ventilator
• Precaution:
  – If ET tube pulled out, it may cause injury to the vocal cords.
• What to do if pulled out:
  – Check patients breathing, apply O₂/artificially breathe for patient until re-intubated.
**Ventilator**

- **Purpose:**
  - Mechanical device for artificial ventilation of the lungs
- **Activity:**
  - Pt's needing ventilator assist may be able to ambulate
  - Be careful with pts on a lot of support of the ventilator i.e. 100% O₂
  - Be careful not to lean on ventilator "hoses"
- **Other:**
  - Respiratory Therapists can be helpful with any questions you may have about the ventilator

**Ambu Bag**

- **Purpose:**
  - Manually ventilate pts with tracheostomy or endotracheal tubes, stimulate a cough, supplement O₂ & ↑ volume of air during breathing
- **Activity:**
  - For pt. ambulation if portable ventilator not available or suctioning

**Tracheostomy Tube**

- **Purpose:**
  - Artificial airway in the trachea that aids in breathing & protecting the airway. Performed to ↓ tracheal or vocal cord injury. Usually for pts needing prolonged intubation.
- **If accidentally removed:**
  - Check pt's breathing, apply O₂/artificially breathe for patient until tracheostomy tube is put back in.
- **Other:**
  - If not yet consulted, check with your friendly SLP about swallowing, electro-larynx etc.

**Trach Collar**

- **O₂ delivery system via high humidity**
  - Humidity needed to warm and add moisture
  - FiO₂ ranges from 21-100% depending upon the patient's need
- **Activity:**
  - Can use venturi system for ambulation
Passy Muir Speaking Valve

**Passy Muir Speaking Valve (PMSV)**

- **Purpose:**
  - Restore verbal communication skills of a patient requiring a trach.
  - Also assists in coughing up secretions.

- **Precautions:**
  - The cuff on the trach must be deflated when the speaking valve is on otherwise the patient cannot breathe.
  - It is ok to remove the PMSV if a patient desats during activity/procedure. When the patient recovers (i.e. SpO₂ or no longer SOB), replace the PMSV.
  - Patients must maintain SpO₂ >90% in order to wear the PMSV all day.
  - The patient must be on high humidity trach collar (HHTC) prior to receiving a speaking valve assessment.

Suctioning

**Suctioning**

- **Purpose:**
  - To aide patient in removing secretions

- **Precaution:**
  - Do not hold suction for more than 10 seconds and watch HR

- **Activity:**
  - To improve exercise tolerance, removal of secretions may 1st be needed
  - Pt. may need hyper-oxygenation or hyperventilation during suctioning process

The FDA states...

“medical oxygen is defined as a prescription drug which requires a prescription in order to be dispensed except...for emergency use.”

1Reference: Section 503(b) (4) of the Food, Drug, and Cosmetic Act; 21 CFR Sections 201.(b)(1) and 211.130.

Basics of O₂ Use and Titration of Oxygen

Rohini Chandrashekar, PT, CCS
Christiane Perme, PT, CCS
OXYGEN PRESCRIPTION

• Supplemental oxygen therapy orders are generally for continuous administration.
• During a physical therapy intervention, a physician’s order is required to provide, remove or titrate supplemental oxygen.
• A PRN order may be entered for specific situations such as exercise, chest pain, during sleep.

Oxygen Prescription

• The physician’s order may include: (2)
  – Flow rate or inspired oxygen concentration (FiO₂)
  – Specified target pulse oxygen saturation (SpO₂%).
  – Oxygen delivery device
  – Oxygen weaning parameters.

PHYSICAL THERAPY - RESPONSIBILITIES

• Physical therapists discussing the oxygen needs of their patients with physicians should request orders using an SpO₂% threshold in order to ensure safety and effectiveness during physical activity and exercise. (3)

• If the physician prescribes a specific oxygen saturation (SpO₂) target level during rest and activity (e.g., “maintain SpO₂ > ____ %”), physical therapists may titrate the oxygen flow to maintain patients at or above this target saturation value.

DETERMINATION OF NEED FOR SUPPLEMENTAL OXYGEN

• The patient may have normal saturation at rest but desaturates with the onset of exercise/activity. In most cases supplemental oxygen is indicated when the SpO₂ is <88%.

  Recommendation: Increase oxygen with activity; decrease oxygen at rest. Request orders before next intervention.

DETERMINATION OF NEED FOR SUPPLEMENTAL OXYGEN

• Change in respiratory rate and pattern of breathing.

  Recommendation: Employ breathing retraining. If unsuccessful increase level of supplemental oxygen. Request orders.
DETERMINATION OF NEED FOR SUPPLEMENTAL OXYGEN

• Patient complaints of dyspnea with drop in oxygen saturation

Recommendation: If rest and breathing techniques are unsuccessful, increase level of supplemental oxygen. Request orders.

DETERMINATION OF NEED FOR SUPPLEMENTAL OXYGEN

• Change in heart rate or change in rhythm

Recommendation: If there is a consistent, rapid and sustained elevation in the heart rate at rest or on minimal exertion request physician evaluation not just orders for oxygen.

DETERMINATION OF NEED FOR SUPPLEMENTAL OXYGEN

• Patients with a diagnosis of cardiac compromise eg. Congestive heart failure, may be prescribed supplemental oxygen even in the presence of “normal” oxygen saturation

Recommendation: Do not titrate oxygen to lower levels. Follow prescription.

OXYGEN TITRATION

• When requesting an order to provide oxygen during physical therapy it is recommended that the order specifies the SpO₂ % to be maintained during rest and activity. This allows the physical therapist to “titrate” the level of supplemental oxygen during interventions.

How low can the oxygen saturation go??

OXYGEN TITRATION

• Once the level of supplemental oxygen for a particular activity is “titrated” it is important to communicate this value to the physician and document in your notes.

How low did the oxygen saturation go?? How much oxygen did the patient need??

IMPORTANT CONSIDERATIONS PRIOR TO PHYSICAL THERAPY.

• The delivery system providing the supplemental oxygen must be evaluated
  – Type e.g. cannula, venti mask, non rebreather mask, tracheostomy collar, ventilator
  – If an artificial airway is in place, it must be secured
  – Liter flow and /or Fraction of inspired oxygen (FiO₂) expressed as a percentage
  – The oxygen tank must be checked to ensure that an adequate amount will be available throughout the treatment.
IMPORTANT CONSIDERATIONS PRIOR TO PHYSICAL THERAPY IN ACUTE CARE

• Establish an effective communication strategy since patients with artificial airways are unable to talk. An exception would be patients on T-collar who can tolerate the use of a Passy-Muir valve during activities.
• Check the length and security of all lines and tubes
• A gait belt must be used for all transfers and walking re-education activities
• A wheelchair must be available to allow for resting periods and safe return to bedside if needed

GUIDELINES DURING PHYSICAL THERAPY INTERVENTION

• The physical therapy intervention should be initiated once the order for supplemental oxygen has been verified, and the oxygen delivery device checked out.
• When using the finger pulse oximeter it is important to correlate the heart rate values seen on the probe with the actual heart rate in order to verify the accuracy of the reading.
• Depending on the severity of the illness and the progression in physical therapy, monitoring of oxygen saturations may be continuous or intermittent during the exercise session.

GUIDELINES DURING PHYSICAL THERAPY INTERVENTION

• Additional pulse oximetry may be performed on an as needed basis based on clinical assessment of signs and symptoms of respiratory distress or patient complaints of chest pain, dizziness or any symptoms which may indicate cardiopulmonary distress.

GUIDELINES DURING PHYSICAL THERAPY INTERVENTION

• Physical therapy interventions which can help raise oxygen saturation to the acceptable level must be attempted before increasing the level of supplemental oxygen.

At the end of the physical therapy intervention place the patient must be placed back on the amount of supplemental oxygen and delivery device prescribed when at rest!

DOCUMENTATION

• When documenting oxygen saturation, include oxygen delivery system as well as the amount of supplemental oxygen the patient requires
• Note how long the patient could tolerate a specific activity before desaturation
• Note the time it took for the patient to recover to optimal saturation levels
• Note the interventions that assisted the patient in raising SpO2% and / or decrease symptoms of dyspnea
• Document all vitals pre and post physical therapy intervention

Oxygen Delivery in the Acute Care Setting
Amy Pawlik, PT, DPT, CCS
Chris Perme, PT, CCS
**OXYGEN THERAPY IN ACUTE CARE**

One more time....

*Oxygen therapy is the administration of oxygen at concentrations greater than ambient air with the intent of treating or preventing the symptoms and manifestations of hypoxia*

**Indications**

- Documented hypoxemia
  - PaO2<60, SpO2<90
- Suspected hypoxemia
  - Substantiated in appropriate time frame
- Severe trauma
- Acute MI
- Short-term therapy (ie: post-anesthesia)
- Post-surgical

**Decision tree in acute COPD**

[Diagram of decision tree]

AARC guidelines. 2002

**ACUTE CARE-Assessment of need for Oxygen therapy**

- Need is determined by measurement of inadequate oxygen saturations by:
  - Invasive or noninvasive methods and/or
  - Presence of clinical indicators
- Supplemental oxygen flow should be titrated to maintain adequate oxygen saturation as indicated by:
  - Pulse oximetry
  - Appropriate arterial or venous blood gas values

**OXYGEN THERAPY IN ACUTE CARE**

- Some patients may not qualify for oxygen therapy at rest but will qualify for oxygen during ambulation, sleep, or exercise
- Oxygen therapy is indicated during these specific activities when the saturations falls to less than 88% or otherwise ordered by the MD

**Emergency Care**

- Emergency Care
- Intensive Care Unit
- Intermediate Care
- Acute care floor
- Long term acute care
OXYGEN THERAPY IN ACUTE CARE - PEDIATRIC X ADULT

The administration of supplemental oxygen to neonatal and pediatric patients requires the selection of an oxygen delivery system that suits the patient’s size, needs, and the therapeutic goals.

Modes of Delivery

• High and low flow devices (as previously discussed)

• Devices unique to acute setting
  – High-flow nasal cannula
  – Mechanical ventilation

High-flow nasal cannula

• Delivers more concentrated flow of oxygen, up to 100% FiO₂ and 60 L/min
• Also provides positive end expiratory pressure (PEEP) to improve gas exchange
• The oxygen is typically humidified to increase comfort
• Can be used as an alternative to face mask to allow patient to eat, drink, and talk
• Oxygen tanks only last ~15 minutes, so ensure you use a full tank if walking the patient
• Frequently seen in patients with pulmonary fibrosis, severe lung disease, or in infants

Mechanical Ventilation

WHAT DO PHYSICAL THERAPISTS NEED TO KNOW TO WORK IN ICU?

• Basic cardiopulmonary physiology
• Basic pathophysiology of pulmonary disease
• Mechanical ventilation
• Artificial airways
• Arterial blood gases
• Oxygen delivery systems

MV settings

• Parameters set in ALL modes of MV (oxygenation)
  – Fraction of Inspired Oxygen (FiO₂)
  – Positive end-expiratory pressure (PEEP)

• May be set, depending on mode (ventilation)
  – Rate
  – Volume
  – Pressure
OXYGEN THERAPY IN ACUTE CARE-MONITORING

• Clinical assessment should include, but is not limited to:
  – Cardiac, pulmonary, and neurologic status
  – Work of breathing
  – Oxygen saturation

OXYGEN THERAPY IN ACUTE CARE-Monitoring during physical therapy

• Clinical assessment should be performed by the clinician to determine changes in clinical status (e.g., dyspnea scales)
• Baseline oxygen saturation must be measured before any activity is begun
• Oxygen saturation measurements should be done continuously or when clinically indicated

OXYGEN THERAPY IN ACUTE CARE-Infection Control

• Normally, low-flow oxygen systems without humidifiers do not present a clinically important risk of infection.
• High-flow systems that employ heated humidifiers or aerosol generators, especially when applied to patients with artificial airways, should be cleaned and disinfected on a regular basis.

* For a complete copy of this guideline, see Resp Care 37:918-922, 1992

GUIDELINES DURING PHYSICAL THERAPY INTERVENTION

At the end of the physical therapy intervention place the patient must be placed back on the amount of supplemental oxygen and delivery device prescribed when at rest!

Oxygen in Acute Care

Oxygen Protocols???

• Many facilities have their own policies/protocols regarding O2 use
  – Initiation
  – Titration
  – Devices
Oxygen Use in Individuals with COPD and CO2 Retention

Ellen Hillegass, PT, EdD, CCS

Benefits of LTOT for COPD

Overall Benefits:
- Improve survival in COPD pts with chronic RF
- Reduce number of hospitalizations
- Increase exercise tolerance
- Improve quality of life

Criteria for LTOT
- PaO2 < 60 mm Hg
- Stable clinical situation
- Receiving optimal pharmacological treatment
- Should be prescribed for at least 18 hrs/day


Specific Benefits:
- Decreases pulmonary hypertension or stabilization of PAH
- Decreases red cell mass
- Increases exercise capacity
- Reduction in exacerbations
- Fewer cardiac arrhythmias and ECG findings associated with myocardial ischemia
- Improvement in neuropsychiatric function

Clinical Benefits
- Clinical benefits of LTOT depend on:
  - Treatment compliance
  - Duration of treatment
  - Adequate correction of hypoxemia


Indications for LTOT in COPD (U.S.)
- PaO2 < 55 mmHg or SpO2 < 88% (Room air)
- PaO2 56-59 mmHg or SpO2 89-90% WITH (≥1)
  - Pulmonary hypertension
  - Evidence of cor pulmonale or edema due to HF
  - Elevated hematocrit (>56%)

Is LTOT for everyone?
- NOTT & MRC: PaO2 < 60 mm Hg
- Gorecka 1997 : no benefit on survival in COPD with moderate hypoxemia (56-60 mm Hg)
- Results of other trials: LTOT benefits COPD pts in other ways....
  - Therefore survival NOT best outcome to observe benefits of LTOT

Cooper 1993
How to assess eligibility for LTOT?

- ABGs should be performed 2x to confirm criteria for LTOT
  - In clinical situation LTOT usually prescribed while patient is unstable or after only single assessment
  - Guyatt (2005) found significant number of LTOT pts were ineligible for LTOT during followup (<3 mos)

Does prescribed O2 adequately correct O2 saturation?

- O2 flow should be titrated during daytime as patient is clinically stable.
  - Set O2 flow to achieve SpO2 ≥ 90%
  - Overnight pulse oximetry should be recorded during sleep to assess nocturnal SpO2
- During exercise:
  - No specific recommendations
  - Assess adequate O2 flow to correct O2 saturation until SpO2 ≥ 90%
  - 6MWT is good reflection of desaturation during daily activities
  - Morante 2005

Does prescribed O2 adequately correct O2 saturation?

- During sleep:
  - Sleep hypoventilation (SH) has been observed in high % of patients
    - May or may not be due to oxygen therapy
    - Increasing O2 at night may exacerbate the hypoventilation (O’Donoghue 2003, Tarrega 2002)
    - Samokh 2008 increased nocturnal flow by 1 liter: increased SH and respiratory acidosis.
  - Need exists to titrate O2 at night as during exercise: evaluate on an individual basis

What is the Concern of O2 in individuals with COPD

- Worsening CO2 retention and respiratory acidosis when O2 administered to patients with elevated PCO2
  - Belief is that this will cause a blunting of hypoxic ventilatory drive and result in hypoventilation
  - 100% oxygen provided noninvasively to COPD patients with Acute Respiratory Failure
    - Resulted in acute 18% decrease in VE
    - After 15 minutes of breathing 100% O2 VE returned to 93% baseline value with breathing room air
    - PCO2 inc 23mm Hg: 48% attributed to deadspace ventilation
    - Acute administration of increased O2 did cause hypercapnia due to hypoxic vasoconstriction in underventilated lung
      - V/Q mismatch increased
    - NOT due to hypoventilation
      - Aubier: Am Rev Respir Disease 1980

What is risk of CO2 retention?

- Moloney 2001
  - Individuals with acute exacerbation of COPD and hypercapnia with respiratory failure
  - 3/24 developed CO2 retention with controlled O2 provided by Venturi mask to maintain SpO2 91-92%
    - Defined as rise in pCO2 of > 7.5 mm Hg
    - Presented with more severe hypercapnia

Recommendations with CO2 retainers

- Titrate O2 with activity if desaturation occurs with activity
- Watch for signs of exercise intolerance or lack of response to increased O2
  - SpO2 does not increase or even decreases
  - OR exercise intolerance
  - Other VS do not respond appropriately
  - Signs of cognitive or motor impairment or increased dyspnea
Oxygen Use in Cystic Fibrosis

Susan Butler McNamara, PT, MMSc, CCS

Cystic Fibrosis

- Most common and lethal genetic disease in U.S.
- Autosomal recessive
  - 5% carrier rate
- 1 in 3500 live births
  - Average 1000 new cases annually
- Multisystem: involves epithelial cells of exocrine glands
- “Salty Kiss”
- Acute or persistent respiratory symptoms
- Failure to thrive
- Malabsorption
- Meconium ileus
- Recurrent sinus infections

Cystic Fibrosis

- Greater than 45% individuals with CF over 18 years
- Emphasis on preventive and long term care
- Importance of physical fitness and exercise at all levels of disease

Cystic Fibrosis Median Life Expectancy

Graph showing Median Life Expectancy for Cystic Fibrosis from 1940 to 2008.

Average Lung Function Decline

Graph showing average lung function decline with age from 10 to 80 years.
Exercise: early studies

- Cerny et al: 1984: Airway clearance vs. Exercise
- Nixon et al: 1992: Patients with ≥ 82% VO\textsubscript{2} Max = 83% survival and 3 x more likely to survive
- Marcus et al: 1992: Supplemental Oxygen increased exercise duration by decreasing oxygen desaturation with exercise

Exercise

- Adjunct for airway clearance
- Improves ventilatory muscle strength and endurance
- Improves bone health
- Improves overall fitness
- May improve self-esteem
- Increased exercise endurance

Oxygen Therapy and Cystic Fibrosis

- Decreases arterial hypoxemia
- Reduces work of breathing/subjective dyspnea
- Prevents development/progression pulmonary hypertension
- Increases O\textsubscript{2} delivery to working muscles
- Delay onset of anerobic threshold

CF Adult Care Consensus Report: Supplemental O\textsubscript{2}

- Preventative measure for pulmonary hypertension
- Minimize arterial hypoxemia
  - Sleep: SpO\textsubscript{2} less than 88-90% for ≥10% sleep cycle
  - Exercise: SpO\textsubscript{2} less than 88-90%

Evidence for Oxygen Therapy and Cystic Fibrosis

- McKone et al: 2002: effects of supplemental oxygen on submaximal exercise: n=3, moderate to severe disease
- Elphick, Mallory: 2009: Cochrane Review:
  - Use for patients with objective signs of hypoxemia (exercise or sleep; rest/awake);
  - Use in advanced lung disease and hypoxemia with exercise
Determination of Oxygen Therapy in Cystic Fibrosis

- Use of 6 minute walk test, shuttle test or submaximal test
  - Simulates level of ADL's
  - Able to determine training heart rate range
  - Identify level of activity in which oxygen desaturation occurs/not
  - Estimate need for supplemental oxygen

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Objectives

- Briefly review the pathophysiological manifestations of heart failure most related to oxygenation
- Briefly review the available literature examining the effects of supplemental oxygen at rest and during exercise in patients with heart failure
- Briefly review a case study demonstrating the effects of supplemental oxygen and dobutamine on oxygenation and functional capacity

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Oxygen Therapy for Patients with Heart Failure

Lawrence P. Cahalin PhD, PT, CCS
Bouvé College of Health Sciences, Northeastern University
Brigham & Women’s Hospital
Boston, Massachusetts

Left Sided Heart Failure
VE-VCO₂ Relationship

- VE/VCO₂ slope elevated in HF
  - Chua et al., 1997; Reindl et al., 1996
- Related to poor pulmonary perfusion
  - Banning et al., 1995; Wada et al., 1993
- Negatively correlated with:
  - Cardiac output response to exercise
  - Myers et al., 1999; Reindl et al., 1996
- Positively correlated with:
  - Mean pulmonary artery pressure and pulmonary vascular resistance
  - Reindl et al., 1996

Studies Directly Examining Oxygenation or the Effects of Supplemental Oxygen in Patients with Heart Failure at Rest

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Measurements</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubin et al</td>
<td>15</td>
<td>PaO₂</td>
<td>PaO₂ was normal (81.3±8 mm Hg) at rest in patients with severe heart failure</td>
</tr>
<tr>
<td>Munger et al</td>
<td>10</td>
<td>Numerous indices of SpO₂</td>
<td>Improved in CSR, SpO₂, and sleep with O₂ therapy</td>
</tr>
<tr>
<td>Harly et al</td>
<td>9</td>
<td>CSR, SpO₂, sleep</td>
<td>Improvement in CSR, SpO₂, and HVR with O₂ therapy</td>
</tr>
<tr>
<td>Andreas et al</td>
<td>20</td>
<td>CSR, SpO₂, HVR</td>
<td>100% O₂ increased PCWP, SVR, PVR, and SV and decreased SV and CO with lower levels of O₂ (24% &amp; 40%)</td>
</tr>
<tr>
<td>Haqua et al</td>
<td>10</td>
<td>HR, MAP, SV, CO, PCWP</td>
<td>Decreasing the breathing frequency and controlled breathing improved SpO₂ and exercise performance</td>
</tr>
<tr>
<td>Andreas et al</td>
<td>20</td>
<td>SpO₂, MSNA</td>
<td>Similar improvement in AH and SpO₂ indices during apnea</td>
</tr>
<tr>
<td>Krachman et al</td>
<td>25</td>
<td>SpO₂ indices, AH</td>
<td>Improvement in SpO₂ and MSNA during apnea</td>
</tr>
</tbody>
</table>

CSR=Cheyne-Stokes respiration; SpO₂=oxygen saturation; HVR=hypercapnic ventilatory response; SV=stroke volume; CO=cardiac output; PCWP=pulmonary capillary wedge pressure; SVR=systemic vascular resistance; PVR=pulmonary vascular resistance; MSNA=muscle sympathetic nerve activity; AH=apnea/hypopnea index.

Studies Directly Examining Oxygenation or the Effects of Supplemental Oxygen in Patients with Heart Failure During Exercise

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<td>Rubin et al</td>
<td>15</td>
<td>PaO₂</td>
<td>PaO₂ increased from 81.3±8 mm Hg to 90±14 mm Hg during exercise in patients with severe heart failure</td>
</tr>
<tr>
<td>Resnick et al</td>
<td>12</td>
<td>SpO₂, SMWT</td>
<td>SpO₂ decreased from 94.4% to 90.1% and 2 L/min of O₂ increased SpO₂, but did not improve the decrease in paO₂ during the SMWT. However, 4 L/min of O₂ during endurance walking improved the minimum SpO₂ from 90.4% to 93.1%. The SMWT and endurance walking distance were not improved with O₂ therapy.</td>
</tr>
<tr>
<td>Bernardi et al</td>
<td>15</td>
<td>SpO₂</td>
<td>Decreasing the breathing frequency and controlled breathing improved SpO₂ and exercise performance</td>
</tr>
<tr>
<td>Howe-Exquel &amp; Shrop</td>
<td>44</td>
<td>SpO₂, SMWT</td>
<td>Decreasing the breathing frequency and controlled breathing improved SpO₂ and exercise performance</td>
</tr>
<tr>
<td>Lau et al</td>
<td>8</td>
<td>SpO₂, SV, CO</td>
<td>SpO₂ decreased from 98.5% to 95.5%</td>
</tr>
<tr>
<td>Smith et al</td>
<td>24</td>
<td>SpO₂, DLCO, Or</td>
<td>DLCO/CO was decreased at rest and during exercise, but SpO₂ decreased only slightly and similar to a control group. Patients with PAH demonstrated a significant decrease in paO₂, but the SpO₂ of patients with heart failure decreased only slightly. Although no significant change in SpO₂ in patients with heart failure, functional status was significantly related to SpO₂.</td>
</tr>
<tr>
<td>Debrock et al</td>
<td>19</td>
<td>SpO₂, VO₂ indices</td>
<td>Patients with PAH demonstrated a significant decrease in paO₂, but the SpO₂ of patients with heart failure decreased only slightly. Although no significant change in SpO₂ in patients with heart failure, functional status was significantly related to SpO₂.</td>
</tr>
<tr>
<td>Schauer et al</td>
<td>12</td>
<td>SpO₂, SMWT</td>
<td>Decreasing the breathing frequency and controlled breathing improved SpO₂ and exercise performance</td>
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</tbody>
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SpO₂=oxyhemoglobin saturation; SMWT=six minute walk test; SV=stroke volume; CO=cardiac output; DLCO=diffusion capacity for carbon monoxide; Or=pulmonary blood flow; PAH=pulmonary arterial hypertension.
**Obstructive Pulmonary Disease**

**Studies Examining the Effects of COPD Upon Cardiorespiratory Indices in Patients with Heart Failure at Rest and During Exercise**

<table>
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<tbody>
<tr>
<td>Guazzi et al</td>
<td>138</td>
<td>Cardiorespiratory Indices</td>
<td>Patients with both COPD and HF had significantly poorer PFTs, peak VO2, VE/CO2 slope, and heart rate recovery compared to patients with HF alone.</td>
</tr>
</tbody>
</table>

**Case Study**

67 y/o man with de-compensated heart failure

- Admitted six times for ADHF over the past year
- PFTs revealed a mixed restrictive & obstructive deficit with poor DLCO (FEV1 & FVC were 34% of predicted)
- Smoking history of 120 pack years
- 2 L supplemental O₂

**Summary**

- At rest, low levels of supplemental oxygen appear to mostly improve oxygenation and several other indices (e.g. sleep, Cheyne-Stokes breathing, apnea)
  - CPAP and BiPAP?
- During exercise, supplemental oxygen appear to have the potential to improve oxygenation
  - Pulmonary hypertension and COPD?
- Improving cardiac function is most likely to improve the ventilation, oxygenation, and functional status of patients with heart failure
- More research is needed – especially the effects of COPD & diastolic dysfunction on oxygenation in heart failure

**Conditions of Decreased Lung Tissue Compliance**

- **Pulmonary Causes**
  - IPF
  - Asbestosis
  - Coal Workers’ Pneumoconiosis
  - Bronchitis Obliterans
  - Pneumonia
  - Pleural Effusions
  - Sarcoidosis
  - ARDS
- **Connective Tissue Causes**
  - Rheumatoid Arthritis (RA), Systemic Lupus Erythematosis (SLE), Scleroderma, Polymyositis
- **Iatrogenic**
  - Drugs i.e. chemotherapy, amiodarone (cardiac med)
  - Radiation therapy

**O₂ use in Interstitial Lung Disease and in Pulmonary Arterial Hypertension**

Amy Pawlik, PT, DPT, CCS
Rebecca Crouch, PT, DPT, CCS
Prevalence (US)

- Sarcoidosis: 54,000
- IPF: 20/100,000 (male), 13/100,000 (female) Roughly = 62,100
- COPD: 12.1 million!

Am J Respir Crit Care Med. 2000; 161(2): 646-64.

7 Classic Clinical Signs

1. Tachypnea
2. Hypoxemia (V/Q mismatching)
3. Dry Inspiratory Crackles
4. Decreased Lung Volumes
5. Decreased Diffusion Capacity (DLco)
6. Cor Pulmonale (pulmonary HTN)
7. Other Possible Signs: altered CXR; digital clubbing; cyanosis; decreased chest wall expansion
3 Hallmark Symptoms

1. Dyspnea (RR, shallow breathing)
   -- Has difficulty getting air

2. Cough (irritating, dry, non-productive, may be in response to low SpO2)

3. Possible wasted, emaciated appearance
   a. High caloric expenditure 24h/day due to Work Of Breathing
   b. Since breathing is hard work, eating is more difficult
   c. Appetite often decreased

Exercise Intolerance

• Circulatory
  -- PAH

• Peripheral muscle weakness
  -- Disuse
  -- Corticosteroids

• Respiratory mechanics
  -- Ventilation
  -- Oxygenation

Respiratory Mechanics

• Shallow, rapid breathing pattern
  -- Worsens with activity

• Not ventilatory

• Impaired gas exchange (ref?)

Impaired gas exchange

• Destruction of pulmonary capillary bed

• Thickening of alveolar-capillary membrane

• Leading to
  -- V/Q mismatch
  -- Limitation to oxygen diffusion
  -- Low mixed venous PO2

Indications for use of O2

• Resting PaO2 <55mmHg with breathlessness

• Breathless, mobile with SpO2 < 88-90% with exercise

• No evidence that long-term O2 therapy is associated with improved survival in ILD and hypoxia

 Thorax 2008 ILD Guidelines

Supplemental O2 and ILD

• Increases
  -- Exercise duration
  -- Maximum work load


What about Breathing Re-Training?

**Pros**
- Slows respiratory rate
- Improves gas exchange to increase saturation
- Improves chest mobility
- Preserves diaphragmatic strength and coordination

**Cons**
- Impossible to accomplish due to rapid RR
- Doesn’t do any good—can’t maintain this pattern at rest much less with exercise
- Causes more patient stress than it’s worth
- Don’t try to beat a dead horse

Pulmonary Arterial Hypertension (PAH)

**Pros**
- Poor exchange of gases due to vascular abnormality
- Marked desaturation at rest and with exercise

Ominous Clinical Symptoms of PAH

- Chest pain
- Light-headedness
- Low oxygen saturation
- Sudden death!

Management of PAH

**Treatment**
- Supplemental oxygen
- Potent vaso-dilators
  - IV
    - Flolan
  - Oral
    - Revatio
  - Inhaled
    - Ventavis

**Clinical Guidelines in treated PAH patients**
- Avoid FALLS!
- Avoid Valsalva maneuver
- Avoid isometric exercise
- Maintain higher SpO2 levels
- Low level weight training is acceptable
- Isotonic/continuous/aerobic exercise is acceptable—even at higher workloads
- Exercise testing and exercise training is safe with proper monitoring

Exercise and ILD and PAH

- Patients...receiving long-term oxygen therapy should have this continued during exercise training, but may require increased flow rates*
- May see dramatic drops in O2 saturation
- Patients may require large amounts of supplemental O2, often from two sources**

Summary

Ann Fick, PT, DPT, CCS

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*ATS/ERS Statement on PAH. Am J Respir Crit Care Med. 2006;173:1390-1413

Recommended Studies: NHLBI

- O2 supplementation during ambulation
- Continuous oxygen supplementation in patients with moderate hypoxemia
- Nocturnal O2 treatment of desaturation during sleep
- Detailed individualized Prescriptions for long-term oxygen supplementation
- Need to look at different outcome measures; not just mortality
  - Exercise capability
  - Sleep quality
  - Rate of exacerbations,
  - Quality of life
  - Mood
  - Cognitive function
  - Health care utilization


Recommendations

- Remember hypoxemia has several physiologic consequences
  - Watch for signs and symptoms of hypoxemia
  - MONITOR with pulse oximeter, but keep in mind errors with pulse oximetry and monitor all VS
  - Investigate your institution’s guidelines for O2 use
- Learn about O2 delivery systems, become familiar with them and expand your experience with use of oxygen and different systems

Future Steps

- Position Paper to follow
- Work with APTA to increase PT knowledge of O2 use

Thank You

References

- CrinerGJ. Effects of long-term oxygen therapy on mortality and morbidity. Respir Care. 200;45;105-18.
## References


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## References

