Objectives

1. Understand the definition of OHS.
2. Review the patho of ventilation control and its relation to OHS.
3. Recognize clinical manifestations, morbidity and mortality.
4. Identify tests used for diagnosis and diagnostic criteria.
5. Describe different treatment options for OHS.
7. Discuss important follow-up issues.

Obesity

- ...is common, serious and costly
- In 2008, 33.8% of men & women were obese. 2,1
- $147 billion dollars spent in 2008 for medical costs of obesity 1,2
- Annual health costs for obese patients are 36% greater than health costs as compared to patients with normal BMI. 3
Obesity Trends* Among U.S. Adults
BRFSS, 1985
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 1987
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 1990
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1992
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5' 4" person)

Source: Behavioral Risk Factor Surveillance System, CDC.

Obesity Trends* Among U.S. Adults
BRFSS, 1994
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5' 4" person)

Source: Behavioral Risk Factor Surveillance System, CDC.

Obesity Trends* Among U.S. Adults
BRFSS, 1996
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5' 4" person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1999
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 2001
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 2004
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2005
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 2007
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Obesity Trends* Among U.S. Adults
BRFSS, 2009
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2010
(*BMI ≥ 30, or ~ 30 lbs. overweight for 5’4” person)

Obesity Complications
- Type 2 diabetes
- Hypertension
- Heart disease
- Sleep apnea
- Obesity hypoventilation syndrome
- Abnormal respiratory mechanics
- Stroke
- Liver/gallbladder disease
- Osteoarthritis
- Gynecologic problems
- Dyslipidemia
- Cancers
- Psychiatric

Obesity & Respiratory
- Higher risk for
  - aspiration pneumonia
  - respiratory failure
  - pulmonary embolism
  - sleep apnea
  - obesity hypoventilation
  - Asthma*
  - COPD*
**Obesity & Respiratory**

- Specific respiratory complications 
  - exertional dyspnea
  - decreased lung volumes
  - restrictive defect on PFT
    - (FVC and normal FEV1/FVC ratio; >70)
  - decreased chest wall compliance/increased airway resistance
  - adipose tissue hinders diaphragmatic movement
  - diminishes basal lung expansion
  - hypoxemia and CO2 retention
  - decrease respiratory muscle endurance

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**Central vs Peripheral Obesity**

- Central adiposity
  - More common in males
  - Associated with worse lung function and respiratory symptoms

- Peripheral adiposity
  - Fewer medical complications
  - Better lung function

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**Control of Ventilation: A Review**

- Ventilation changes in response to
  - Arterial PCO2, PO2 and pH
  - Mechanical or irritant stimuli
  - Neural and chemical receptors
Neural and Chemoreceptors

- Thoracic neural receptors
  - Present in upper airways, trachea, lung, chest wall and pulmonary vessels.
  - Respond to changes in lung volumes and presence of chemicals.
  - Signals the respiratory centers via the vagus nerve.
Neural and Chemoreceptors

- Peripheral chemoreceptors
  - Carotid and aortic bodies
  - Sense partial pressure of arterial oxygen
  - Impulses travel through CN IX
  - Increases ventilation

- Central chemoreceptors
  - Medulla and mid-brain
  - Vigorous and instantaneous response to changes in pH of CNS environment.
  - CO2 crosses blood-brain barrier

Alterations in Ventilatory Response

- 15% of adults have diminished response to CO2
  - More likely to develop CO2 retention with additional respiratory problems.
  - Can occur with elevation of serum and ECF bicarbonate
  - CO2 retainers rely more on the hypoxic respiratory drive
Definition

• aka Pickwickian Syndrome
• Obesity (BMI ≥30)
• Chronic alveolar hypoventilation during wakefulness (pCO2 >45mmHg) *In the absence of alternative explanation for hypoventilation
• +/- sleep disordered breathing 22
• +/- hypoxia 18

Pathophysiology of OHS

• Alveolar hypoventilation
• Sleep disordered breathing
• V/Q mismatching
• Excessive load on the respiratory system (obesity)
• Increased work of breathing 14
• Respiratory muscle impairment
• Increased upper airway resistance
• Depressed central ventilatory drive
• Diminished effects of neurohumoral modulators

Predictors of Hypercapnia

• Studies have mixed results
  • Kawata et al 23
  • Severity of Obesity
    • Mean BMI 39
  • Severity of OSA
    • Mean AHI 64
  • Degree of restrictive chest physiology
Sleep Disordered Breathing

- Episodic hypopnea or apnea
- Recurrent partial or complete upper airway obstruction during sleep
- Central hypoventilation
- Often coexists with OHS

- Nocturnal PaCO2 → kidney bicarb to compensate
- Chronically elevated bicarb levels will depress respiratory drive → chronic hypoventilation and hypercapnia day and night

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Sleep Disordered Breathing

- OSA is present in 85-92% of OHS patients

- Severe nocturnal hypoxemia in OSA patients is associated with coexisting OHS. 8, 18

- Correction of OSA eliminates OHS in many patients

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<table>
<thead>
<tr>
<th>Simple Obesity</th>
<th>OSA</th>
<th>OHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>≥ 30</td>
<td>Variable</td>
</tr>
<tr>
<td>Awake PaCO2</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Sleep-Related Breathing Disorder by PSG

- AHI < 5
- AHI > 5
- AHI > 5
  - Sleep hypventilation
  - Increase in PaCO2 > 10 from supine awake values
  - Oxygen desaturations during sleep not explained by apnea or hypopnea
  - Combination OSA and sleep hypventilation

V/Q Mismatching

- Poor ventilation in lower lobes
- Diminished lung compliance
- Difficulty moving rib cage & diaphragm
- Closure of alveoli prior to end expiration

- Increased perfusion in lower lobes
- Increased pulmonary blood volume

- V/Q mismatch causes hypoxemia & hypercapnia

V/Q Mismatching diagram

- Oxygen enters red blood cells
- Capillary
- Red blood cell
- Diffusion of oxygen
- To pulmonary vein
- Epithelium of alveolus
- Carbon dioxide escapes into alveolus
Work of Breathing

- Increased in obesity
  - Due to decreased lung compliance
  - Increased effort to move chest and diaphragm
  - Increased upper airway resistance
- Work of breathing 30% higher in obese, without OHS. 8
- Work of breathing 90% higher in obese, with OHS. 6

Respiratory Muscles & Ventilatory Drive

- Impairment in strength and endurance of respiratory muscles21
  - Generally has to be severe
  - But, with OHS and other contributing factors present, modest impairment is enough
  - May contribute to hypercapnia
- Central ventilatory drive
  - Ventilatory response to chemostimuli
  - Contributes to sustained hypercapnia
  - Improves with PAP therapy21

Neurohumoral Modulators

- Leptin
  - Produced by adipose tissue
  - Acts on receptors in hypothalamus to suppress appetite AND on central respiratory centers to stimulate ventilation. 17
  - Insufficient levels or leptin resistance 8, 19
  - More research needed
Clinical Manifestations

- S/S of coexisting OSA
- S/S of pulmonary hypertension and right sided heart failure/cor pulmonale
- Hypoxemia
- Hypercapnia/Elevated bicarb
- Middle-aged
- 2:1 male-to-female
- Restrictive defect on PFT
- Secondary erythrocytosis
- Possible*
- Systemic hypertension
- Heart failure
- Angina
- Insulin resistance (metabolic syndrome)

Clinical Manifestations

- Difficult to distinguish between OHS & OSA from OSA alone
- DOE
- Severe obesity (usually BMI >50)
Diagnosis
Perform work-up quickly!
Establish the absence of an alternative cause of hypoventilation

ABG
- Hypercapnia (PaCO2 >45mmHg) during wakefulness
- Hypoxemia (PaO2 <70mmHg) usually present
- Pulmonary function testing
  - Rule out obstructive lung disease

Diagnosis
- Chest xray
  - Elevated hemidiaphragms
  - Enlarged heart
- EKG-Echocardiogram
  - Right atrial and right ventricular hypertrophy
  - Pulmonary hypertension
- Lab
  - Thyroid function test
  - Serum electrolytes and bicarbonate
  - CBC

Mokhlesi, B., Tulaimat, A. Recent Advances in Obesity Hypoventilation Syndrome. CHEST 2007; 132;1322-1336.
Diagnosis

- Polysomnography
  - Not required, but should be done
  - Can titrate PAP
  - Monitor severity of desaturations and presence of cardiac symptoms
- Consider work-up for PE

Therapeutic Goals

- Normal acid-base status
  - Improving ventilatory drive
  - Relieving respiratory muscle fatigue
  - Decrease work of breathing
- Prevent oxyhemoglobin desaturation, erythrocytosis & cor pulmonale
  - Normalizing alveolar ventilation
  - Improving V/Q mismatch
  - Correct hypoxemia
- Relieve hypersomnia and altered mentation
  - Treat sleep fragmentation & sleep disordered breathing
  - Restoration of eucapnia

Treatment

- Multidisciplinary & Multifaceted
  - Treatment of comorbid conditions
- Ventilatory support
- Pharmacologic therapy
- Tracheostomy
- Oxygen therapy
- Weight loss
### Ventilatory Support

**Mainstay of therapy**

- **Modes**
  - Continuous positive airway pressure (CPAP)
  - Noninvasive positive pressure ventilation (NIPPV)
    - Bi-level positive airway pressure (BiPAP)
    - Volume cycled positive pressure ventilation (VCPPV)
    - Vent-to-Mask

- Administered via full face mask, nasal mask, nasal pillows or hybrid mask.

### Comparative features of different methods for administering positive pressure

<table>
<thead>
<tr>
<th>Mode of positive pressure ventilation</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td>Inexpensive</td>
<td>Lack of inspiratory pressure support</td>
</tr>
<tr>
<td>Bi-level</td>
<td>Widely available</td>
<td>Tidal volume may be limited by patient-related factors</td>
</tr>
<tr>
<td>Volume-cycled</td>
<td>Can provide inspiratory pressure support to augment tidal volume</td>
<td>More expensive</td>
</tr>
<tr>
<td></td>
<td>Can set specific respiratory parameters</td>
<td>Less widely available</td>
</tr>
</tbody>
</table>

### CPAP

- May benefit patients with coexisting OHS and OSA\(^{1,2}\)
  - Those with higher AHI
  - Less restrictive pathology on PFT
  - Less severe desaturations

- Does not directly augment ventilation
CPAP

- Does not benefit ALL OHS patients
  - Monitor for clinical signs and symptoms that suggest persistent sleep-related hypercapnia
    - Nocturnal dyspnea
    - Sensation of smothering
    - Chronic morning headaches
    - Failure to improve awake ABG
  - Failure to eliminate nocturnal desaturations and/or hypercapnia is indication for BiPAP

NIPPV

- BiPAP
  - Set IPAP and EPAP
  - ↓ nocturnal PaCO2 ↓ daytime PaCO2
  - ↑ long-term survival
    - Helps maintain normocapnia chronically

NIPPV

- BIPAP
  - Advantages
    - Active ventilation vs pneumatic splinting
    - Lower mean airway pressure
    - Rest of ventilatory muscles
    - Rapid improvement in respiratory acidosis
    - Return of normal ventilatory control and chemoreceptor function
    - Can relieve upper airway obstruction while allowing augmentation of tidal volume
    - Better tolerance
NIPPV
• Volume cycled ventilation
  • Hybrid mode
  • Vent-to-Mask*

Lack of Improvement with PAP
• #1 Reason is...
  • Poor compliance with PAP therapy
  • Inadequate PAP titration
  • Sleep disordered breathing, other than OSA (central hypoventilation)
  • Unidentified secondary cause of hypercapnia
  • Chronic metabolic alkalosis

Pharmacologic Therapy
• Progesterone 10
  • Respiratory stimulant
  • Does not address other pathogenic contributors
  • No long-term controlled trials confirming safety/efficacy
  • Side effects
    • Alopecia
    • Decreased libido
    • Uterine bleeding
    • Erectile dysfunction
    • Increased risk of thromboembolism
  • Limited role
Pharmacologic Therapy

- Diamox
  - Causes metabolic acidosis

- Agents to avoid
  - Anything that reduces ventilatory drive or promotes instability of upper airway.
    - Alcohol
    - Benzodiazepines
    - Opiates
    - Barbituates

Tracheostomy

- Relief of upper airway obstruction
  - Still consider other pathogenic factors
  - May still need nocturnal ventilation
  - Possible to have persistent hypoventilation

- Problems
  - Surgery more difficult in obese patients
  - Obesity can limit use of speaking valves
  - Recurrent bronchitis
  - Psychosocial problems
    - Disability, depression, marital discord
  - Rarely used

Oxygen Therapy

- Not recommended as a sole therapy
  - May increase awake PaCO2
  - Does not improve hypercapnia while asleep

- May be used with CPAP or NPPV in OHS

- Distinguish between COPD+OSA and OHS
  - Ideally perform sleep study
Weight Loss

- Benefits
  - Improve ventilation and general health
  - Reduce risk of cardio-respiratory compromise
  - Improvement in desaturations
  - Decreased AHI
  - Resolve pulmonary hypertension
  - Improved LV function
  - Improved pulmonary function
  - Better quality of life

Weight Loss

- Not an exact science

- Controlled and medically supervised weight loss recommended

- Do no delay treatment with PAP in order to determine if weight loss will be beneficial

Weight Loss

- Lifestyle modifications
  - Dietary changes
  - Exercise
  - Behavioral modification
    → largely unsuccessful in the long-term

- Medications
  - Noradrenergic drugs, serotonergic drugs, gastric/pancreatic lipase inhibitor
    → concern for drug induced PH
    → not used as therapy for OHS
Weight Loss

- Bariatric surgery
  - BMI >35 + 2 obesity related comorbidities
  - BMI >40
  - Cooperate with post-operative treatment
  - Avoid pregnancy during rapid weight loss
- Pre-operative sleep study and initiate PAP prior to surgery
- Re-evaluate in 1-2 years after sufficient weight loss has occurred.

Treat Comorbid Conditions

- Multidisciplinary
  - Optimize all affected systems
    - Blood pressure, blood sugar, lipids
  - Heart failure and pulmonary hypertension
    - Right sided, left sided or diastolic dysfunction
  - Erythrocytosis and hyperviscosity
  - COPD
    - Smoking cessation
    - Medical therapy
  - Hypothyroidism
    - Thyroid hormone replacement

Morbidity & Mortality

- Higher mortality rate 13, 18, 21
- Higher rate of hospital & ICU admission and invasive mechanical ventilation 22, 21
- Pulmonary hypertension
- Cor pulmonale
- Lower quality of life
- Higher health care cost and utilization 12
Respiratory Therapy Role

- Very Important!
- Put aside prejudices
- Understand disease and disease process
- **Be a patient advocate and educator**
- Educate other staff (ie, RN, LPN, CNA)
- **Encourage patients with CPAP-BiPAP**
- Monitor clinical signs
- Notify clinician if patient worsens

Follow-Up

- Check awake ABG (bicarb)
- Monitor daytime hypoxia
- Check compliance of ventilation device with smartcard
- Consider ONO with device to ensure nocturnal hypoxia is corrected
- Encourage compliance
- Weight loss activities
- Monitor other comorbid conditions

Conclusions

- Obesity is a growing epidemic
- Increase awareness and treatment of obesity-related diseases
- Pathophysiology is multifactorial
- Early diagnosis and treatment is critical
- Compliance with PAP is vital
- Control other comorbid conditions
- Treatment is multifaceted
- Close follow-up is imperative
Conclusions

- Further investigations and studies are needed
  - To better understand pathophysiology
  - Discover new PAP modalities
  - Explore non-PAP treatment options
  - Improve long-term outcomes of OHS patients

Mr. D Case Study

Age: 59 yo male
Weight: 333 lbs
Ht: 5'11 ½ in
BMI: 45.8

PMH
- Type 2 diabetes
- HTN
- Hyperlipidemia
- Hypertriglyceridemia
- Chronic venous insufficiency

Social Hx
- Lifetime non-smoker
- Etoh 2-3x/week
- No illicit drugs
- Married, 3 kids, local farmer

Mr. D Office Visit Details

Referred to Pulmonology Associates 9/2010
- c/o hypersomnolence (ESS 10) and dyspnea
- ROS negative except…
  - + LE edema
  - + DOE
  - + Fatigue, daytime sleepiness
  - + Weight gain
  - + PND
- Exam
  - BP 128/80, HR 84, T 98.8, R 22, Sp02 94% RA
  - Neck circumference 21.25in
  - Mallampati IV
  - Heart sounds distant, no murmurs
  - Lung CTA
  - 1+ edema LE bilaterally
  - No clubbing or cyanosis
- Plan
  - Sleep Study
  - Lab: TSH, ABG, CBC, BMP, Mg, P04
  - CXR, ECHO, PFT
Mr. D Results

- Sleep Study
  - Split night study, AHI 104 w/ desaturations
  - CPAP @ 14cmH20 with 2L in line
- Lab
  - ABG on RA pH 7.36 PaCO2 49 PaO2 46 HC03 27
  - TSH 0.61
  - Hgb 15, Hct 44, plt 289
  - BMP lytes normal, carbon dioxide 34, glucose 145
- CXR
  - Cardiomegaly without infiltrates or pneumothorax
- PFT
  - Mild restrictive defect, normal lung volume and DLCO
- ECHO
  - Normal EF 65% with LVH
  - Normal PAP, normal right heart function/structure

Mr. D

- Follow-up 3 months
  - “feels good” “don’t fall asleep on the tractor”
  - Usage 100% on SmartCard, ESS 2
  - AHI 1.6, no significant air leak, avg 6hr/night
  - Lost 1lb, 332lbs
- Follow-up 1 year
  - “like my CPAP” “does not nap” “not short of breath”
  - Usage 96.5% on SmartCard, ESS 0
  - AHI 1.1, minor air leak, avg 6hr 20min/night
  - Gained 12lb, 344lbs
  - ONO on CPAP okay
  - Serum carbon dioxide 30
  - Dyspnea improved

- Long-term Goals
  - Weight loss
  - Adequate oxygenation
  - Monitor PaCO2

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Questions??
Thank you!
THE END!