Dyspnea... Mechanisms Assessment Management

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Brain stem
- Respiratory centers -

RESPIRATION
- Act of breathing -

Cerebral cortex
- ? Center -

Rate & Pattern of breathing
Dyspnea

- Greek: *dys*, meaning painful, difficult, and *pneuma*, meaning breath
- Protective function
- Symptom with suffering and disability
- Cardinal symptom of both cardiopulmonary disorder
- Relief of dyspnea → improve QoL
Definitions of dyspnea:

- “difficult, labored, uncomfortable breathing”
- “awareness of respiratory distress”
- “the sensation of feeling breathless or experiencing air hunger”
- “an uncomfortable sensation of breathing”
Wide range of meanings:

1. Subjective complaint without consistency in objective signs such as tachypnea
2. Interpretations represent extrapolations from normal breathlessness (e.g., after strenuous exercise)
3. Most experimental observations relating to dyspnea are based on study of normal subjects or animals under artificial circumstances
4. Loosely applied term, based on experience with predominant patient population (e.g., patients with COPD or asthma)

➢ Despite this variability, in clinical medicine, the complaint of dyspnea almost invariably implies respiratory discomfort.
Dyspnea → amalgam of two components

SENSATION
Sensory input to cerebral cortex from specialized receptors

PERCEPTION
Interpretation of information at sensorimotor cortex
The American Thoracic Society (1999) defines *dyspnea* as a subjective experience of breathing discomfort that consists of qualitatively distinct sensation that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses.
Dyspnea: Clinical Problem

- Common in patients with cardiac or respiratory disease as well as in healthy individuals who are obese and/or deconditioned
- Prevalence of dyspnea in healthy adults (< 65 yrs) ranges from 10 - 18%
- >30% of elderly individuals (≥ 65 years of age) report breathlessness with activities of daily living, including walking on a level surface or up an incline
- Independent predictor of mortality even after adjusting for age, sex, smoking history, and prior occupation*

*Eur J Epidemiol 2001; 17:223-229
Dyspnea Is a Better Predictor of 5-Year Survival Than Airway Obstruction in Patients With COPD

CHEST 2002; 121:1434–1440
A Comparison of the Level of Dyspnea vs Disease Severity in Indicating the Health-Related Quality of Life of Patients With COPD

CHEST 1999; 116:1632–1637
Language of dyspnea

- Dyspnea – subjective sensation
- Cultural or language differences may result in patients using different words to describe the same sensory experience
- Sensation may differ depending on pathophysiology of dyspnea
Example of a List of Descriptors Utilized in Dyspnea Questionnaires

1. My breath does not go in all the way.
2. My breathing requires effort.
3. I feel that I am smothering.
4. I feel a hunger for more air.
5. My breathing is heavy.
6. I cannot take a deep breath.
7. I feel out of breath.
8. My chest feels tight.
9. My breathing requires more work.
10. I feel that I am suffocating.
11. I feel that my breath stops.
12. I am gasping for breath.
13. My chest is constricted.
14. I feel that my breathing is rapid.
15. My breathing is shallow.
16. I feel that I am breathing more.
17. I cannot get enough air.
18. My breath does not go out all the way.
19. My breathing requires more concentration.


*Am Rev Respir Dis.* 1991;144:826-832
Clusters of respiratory sensations described by normal subjects who experienced breathing discomfort in association with a range of respiratory tasks

<table>
<thead>
<tr>
<th>Cluster</th>
<th>BrHo</th>
<th>CO₂</th>
<th>DTV</th>
<th>Res</th>
<th>Elas</th>
<th>FRC</th>
<th>VT</th>
<th>Exer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Rapid</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2. Exhalation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Concentration</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>4. Shallow</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>5. Work</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Suffocating</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Hunger</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>8. Heavy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>9. Gasping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

BrHo = breathholding  
CO₂ = steady state hypercapnia  
DTV = driven targeted ventilation  
Res = resistive load  
Elas = elastic load  
FRC = increased functional residual capacity  
VT = decreased tidal volume  
Exer = exercise

*Am Rev Respir Dis. 1989;140:1021-1027*
# Respiratory Sensations Associated with Various Conditions

<table>
<thead>
<tr>
<th>Sensation</th>
<th>Congestive Heart Failure</th>
<th>Interstitial Lung Disease</th>
<th>Asthma</th>
<th>Neuromuscular and Chest-Wall Disease</th>
<th>Pregnancy</th>
<th>Pulmonary Vascular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid breathing</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete exhalation</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shallow breathing</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased work or effort</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling of suffocation</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air hunger</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest tightness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Heavy breathing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

## Cluster analysis

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Tightness</td>
<td>Asthma (Simon et al., 1990)</td>
</tr>
<tr>
<td>Inability to get a deep breath</td>
<td>COPD</td>
</tr>
<tr>
<td>Unsatisfying Breath</td>
<td>Hyperinflation (O'Donnell et al., 1997)</td>
</tr>
<tr>
<td>Air Hunger</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Urge to Breathe</td>
<td>COPD</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
</tr>
<tr>
<td></td>
<td>Neuromuscular weakness (Simon et al., 1990)</td>
</tr>
<tr>
<td>Heavy Breathing</td>
<td>Peripheral muscle atrophy</td>
</tr>
<tr>
<td>Breathing More</td>
<td>Cardiovascular deconditioning (Mahler et al., 1996)</td>
</tr>
</tbody>
</table>
Problems in study of dyspnea

1. Neural pathways underlying it are not well understood
2. Region of cerebral cortex that processes information related to dyspnea remains unidentified
3. No area of cortex that when stimulated causes dyspnea or any other respiratory sensation, nor is there a cortical lesion that abolishes the sensation of dyspnea or the perception of other respiratory-related stimuli
4. Difficulty in defining the precise physical stimulus that causes it
5. Difficulty in extrapolating experimental studies
Statistical Map Showing Significant Regional Signal Increases Associated with Periods of Air Hunger in an Experiment in which Subjects Were Made Breathless with Acute Hypercapnia in the Setting of Restricted Tidal Volumes

AC = anterior cingulate
In = insula
IPS = intraparietal sulcus
SMA = supplementary motor area
V = cerebellar vermis

Respiratory sensory gating system model

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>Receptors</th>
<th>Locations</th>
<th>Clinical Conditions</th>
<th>Quality of Dyspnea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemoreceptors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in CSF pH</td>
<td>Central Chemoreceptors</td>
<td>Brain Stem (Medulla)</td>
<td></td>
<td>Air Hunger</td>
</tr>
<tr>
<td>Changes in pO₂, pCO₂</td>
<td>Peripheral Chemoreceptors</td>
<td>Carotid and Aortic bodies</td>
<td>CHF</td>
<td></td>
</tr>
<tr>
<td><strong>Mechanoreceptors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stretch Lung Inflation</td>
<td>Pulmonary Stretch Receptors</td>
<td>Pulmonary Alveoli</td>
<td></td>
<td>Chest Tightness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Suffocation</td>
</tr>
<tr>
<td>Tactile Stimulation Air Flow Rate Bronchial Muscle tone</td>
<td>Pulmonary Irritant Receptors</td>
<td>Bronchial Epithelium</td>
<td>Asthma</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Interstitial &amp; Capillary Pressure</td>
<td>C Fibers (JÆJuxta capillary Receptors)</td>
<td>Interstitium Capillaries</td>
<td>CHF, COPD, Pulmonary Vascular Diseases e.g., PE</td>
<td></td>
</tr>
<tr>
<td>Mechanical (movement, length &amp; tension change)</td>
<td>Muscle Spindles</td>
<td>Intercostal Muscles</td>
<td>COPD, Asthma, ILD Neuromuscular diseases</td>
<td>Increased Sense of Effort</td>
</tr>
<tr>
<td>Mechanical (force of contraction)</td>
<td>Tendon Organs</td>
<td>Diaphragm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical (chest wall movement &amp; timing)</td>
<td>Proprioceptors</td>
<td>Joints and Tendons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Physiologic correlate of dyspnea

1. Sense of Respiratory Effort
   - 'air hunger'

2. Chemoreceptors
   - Hypercarbia & hypoxia
   - Urges to breathe
   - Excessive effort
   - Chest tightness

3. Mechanoreceptors
   - Upper airway receptors
   - Lung receptors
   - Vagus nerve
   - Chest wall receptors

Afferent Mismatch / Length tension inappropriateness
Dissociation between dyspnea & respiratory effort

Mean Change in Effort and Breathlessness Rating for Each Subject for Conditions A (PCO2 = 40) and B (PCO2 = 50)

Am Rev Respir Dis 1992; 146:1222-1225
Mechanism of air hunger

Mismatch between automatic drive to breathe and achieved ventilation

Mechanism of sense of effort

sensation arises both from the afferents originating in the working respiratory muscles and from the awareness of outgoing motor command from the motor cortex, as well as perhaps from the medulla (corollary discharge)

Mechanism of chest tightness

- **TIGHTNESS**
- **FOREBRAIN SENSORY AREAS**
- **CHEMORECEPTOR AFFERENT INPUT**
- **MOTOR CORTEX**
- **BRAINSTEM RESP MOTOR CENTERS**
- **RESPIRATORY MUSCLES**
- **VENTILATION**
- **LUNGS**

Intensity of Dyspnea as a Function of Time in Patients Presenting to an Emergency Department with Status Asthmaticus who are Treated with Albuterol at 20 Minute Intervals.

Am J Respir Crit Care Med. 2000;162:490-496
# Dyspnea in Asthma

<table>
<thead>
<tr>
<th>Methacholine induced bronchoconstriction</th>
<th>Dyspnea sensation</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Chest tightness</td>
<td>Bronchoconstriction-induced stimulation of pulmonary receptors</td>
</tr>
<tr>
<td>Moderate</td>
<td>Sense of effort</td>
<td>Increased central motor command associated with the worsening mechanical load on the system</td>
</tr>
<tr>
<td>Severe</td>
<td>Air hunger</td>
<td>Even greater central motor activity</td>
</tr>
</tbody>
</table>
# Dyspnea in Some Common Disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Increased sense of effort</td>
</tr>
<tr>
<td></td>
<td>Stimulation of irritant receptors in airways</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>Increased sense of effort</td>
</tr>
<tr>
<td>COPD</td>
<td>Increased sense of effort</td>
</tr>
<tr>
<td></td>
<td>Hypoxia</td>
</tr>
<tr>
<td></td>
<td>Hypercapnia</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Dynamic airway compression</td>
</tr>
<tr>
<td></td>
<td>Afferent mismatch</td>
</tr>
<tr>
<td></td>
<td>Factors associated with the underlying condition</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Stimulation of pressure receptors in pulmonary vasculature or right atrium</td>
</tr>
</tbody>
</table>
Clinical correlate of dyspnea

- Expiratory flow limitation
- Respiratory muscle weakness
- Decreased lung or chest wall compliance
Respiratory Muscle weakness

- Weakness or mechanical inefficiency of the respiratory muscles results in a mismatch between central respiratory motor output and achieved ventilation.

- Fall in pressure-generating capacity of the respiratory muscles

- Increased ratio of the pressures produced by respiratory muscles to the maximum pressure that can be achieved → worsening dyspnea
Poor respiratory system compliance

- Reduced lung compliance and decreased lung volumes
- Reduced vital capacity and functional residual capacity
- Unable to generate adequate tidal volumes in response to increased neural motor output is likely the basis for the dyspnea and rapid, shallow breathing
Psychologic Effects and Higher Brain Center Influences in dyspnea

- Anxiety, anger, and depression can increase dyspnea out of proportion to the impairment in cardiorespiratory function.

- Quality and intensity of dyspnea at a given level of respiratory activity are also thought to be shaped by patient experience, expectation, behavioral style, and emotional state.

- Relationship between dyspnea and the degree of impairment in lung function is not strong.
The Dyspnea Spiral

Principles and Practice of Pulmonary Rehabilitation
DYSPNEA ASSESSMENT
History

Quality of sensation, timing, positional disposition
Persistent vs. intermittent

Physical examination

General appearance: speak in full sentences? Accessory muscles? Color?
Vitals: tachypnea? Pulsus paradox? Oximetry evidence of desaturation?
Chest: wheezes, rales, rhonchi, diminished breath sounds? Hyperinflated?
Cardiac exam: JVP elevated? Precordial impulse? Gallop? Murmur?
Extremities: edema? Cyanosis?

At this point, diagnosis may be evident, if not Proceed for further evaluation

CXR
Assess cardiac size, evidence of CHF
Assess hyperinflation
Assess for pneumonia, interstitial lung disease, pleural effusions

Suspect low cardiac output, Myocardial ischemia, Pulmonary vascular disease

ECG & ECHO
To assess left ventricular Function and pulmonary artery pressure

Suspect respiratory pump or gas exchange abnormality

PFT- if DLco reduced consider CT
Angiogram to assess ILD & PE

Suspect high Cardiac output

Hematocrit
Thyroid function

If diagnosis uncertain- cardiopulmonary exercise test
## Dyspnea scale: Indirect measurement

<table>
<thead>
<tr>
<th>Scale</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Research</td>
<td>Easy</td>
<td>Difficult following after intervention</td>
</tr>
<tr>
<td>Council (MRC) Oxygen Cost Demand (OCD)</td>
<td></td>
<td>Consider single dimension – magnitude of task</td>
</tr>
<tr>
<td>Baseline Dyspnea Index (BDI)</td>
<td>includes measurement of functional impairment</td>
<td></td>
</tr>
<tr>
<td>Transition Dyspnea Index (TDI)</td>
<td>(the degree to which activities of daily living are impaired) and magnitude of effort (the overall effort exerted to perform activities) and magnitude of task</td>
<td></td>
</tr>
</tbody>
</table>
# Modified Medical Research Council Dyspnea Scale (MMRC Scale)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not troubled with breathlessness except with strenuous exercise</td>
</tr>
<tr>
<td>1</td>
<td>Troubled by shortness of breath when hurrying on the level or walking up a slight hill</td>
</tr>
<tr>
<td>2</td>
<td>Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level</td>
</tr>
<tr>
<td>3</td>
<td>Stops for breath after walking about 100 yards or after a few minutes on the level</td>
</tr>
<tr>
<td>4</td>
<td>Too breathless to leave the house or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

*ATS News 1982; 8:12-16*
Oxygen Cost Diagram

- brisk walking uphill
- medium walking uphill
- slow walking uphill
- bedmaking
- washing yourself
- sitting
- brisk walking on the level
- heavy shopping
- medium walking
- light shopping
- slow walking on the level
- standing
- sleeping

University of California at San Diego
Shortness of Breath Questionnaire (UCSDQ)

- 24-item questionnaire measuring dyspnea during the past week
- Asked about the frequency of dyspnea when performing 21 different activities on a six-point rating scale
- Three additional questions inquire about activity limitations due to shortness of breath, fear of harm from overexertion, and fear of shortness of breath.
- Reliability and validity for the instrument have been reported
Dyspnea scale: Direct measurement

- Cycle ergometry
- 6-min walk test
- Methacholine challenge test
Visual Analogue Scale (VAS)

- 100 mm in length, placed either horizontally or vertically
Dyspnea and Quality of Life: Broadening Conceptions

- Quality-of-life measures are designed to measure how patients function physically, emotionally, socially, and occupationally in their day-to-day lives as a result of their cardiopulmonary disease.
- Improvements in these measures have been shown in some patients to be independent of changes in severity of disease.
- Questionnaires of this type usually appraise dyspnea within the context of a disease that interferes with the individual’s life.
Chronic Respiratory Disease Questionnaire (CRQ)

- 20-item questionnaire evaluating four dimensions of illness: dyspnea, fatigue, emotional function, and mastery
- Each patient is asked to select the five most bothersome activities that elicited breathlessness during the last 2 wk.
- After the patient determines the five most important activities affecting daily life, the severity of breathlessness is determined on a seven-point scale.
- The activities identified are, naturally, unique to the patient and make comparisons of dyspnea scores with other patients difficult.
- Reliability and validity estimates for the CRQ have been reported.
Saint George Respiratory Questionnaire (SGRQ)

- self-administered 76-item questionnaire measuring three areas: symptoms, activity, and impact of disease on daily life.
- Administration time is 20 min.
- Dyspnea is not evaluated specifically but rather included in the symptom category along with information about cough, sputum, and wheezing.
- The SGRQ has been translated into several languages, and reliability and validity estimates have been reported.
Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ)

- Impact of respiratory distress on functional performance of day-to-day activities
- The patient assesses his/her ability to perform various activities as well as the amount of associated dyspnea.
- Dyspnea is also evaluated with three general appraisal questions that create global dyspnea scores that are separate from the score for dyspnea with activity.
- Reliability and validity estimates of the PFSDQ have been reported
Pulmonary Functional Status Scale (PFSS)

- Self administered questionnaire measuring the mental, physical, and social functioning of the patient with COPD
- Dyspnea ratings are obtained in relation to several activities and reflected in a dyspnea subscale.
- Reliability and validity estimates for both scales have been reported.
TREATMENT OF DYSPNEA

- Effectively alleviated by treatment of the underlying disease and its complications

- Focus should be on alleviating symptoms as well as improving pulmonary function

- When dyspnea persists despite optimal treatment of the underlying disease, treatment should focus on the symptom rather than the disease and particularly on the specific mechanisms contributing to an individual's dyspnea
Lung volume reduction surgery for relief of dyspnea in advanced emphysema

- Removal of multiple bullous or emphysematous portions of the lungs reduces hyperinflation and improves lung recoil, potentially leading to dramatic improvement in pulmonary function and dyspnea.

- National Emphysema Therapy Trial (NETT) showed that in patients with heterogeneous emphysema with upper lobe predominance and low exercise tolerance the operation not only relieves dyspnea but prolongs life.

  Thorax 1999; 54:779-789
  Eur Respir J 2002; 19:54-60
REDUCING RESPIRATORY EFFORT AND IMPROVING RESPIRATORY MUSCLE FUNCTION

- Energy conservation techniques reduce physical effort (e.g., walking more slowly) so less ventilatory effort is necessary.
- Breathing techniques (e.g., pursed lips) may reduce respiratory discomfort by slowing breathing and improving oxygen saturation.
- If ventilation limits exercise, strengthening the respiratory muscles should improve maximal ventilation and exercise performance, thereby alleviating the dyspnea.
- Unfortunately the results of this approach have been inconsistent.
Inspiratory Muscle Training in Patients with Chronic Obstructive Pulmonary Disease: The State of the Evidence

Cardiopulmonary Physical Therapy Journal 2009;23:5-15
Supplemental Oxygen - \( \downarrow \) Respiratory Drive

- Supplemental oxygen can reduce carotid body activation, resulting in prolonged breath-holding time.
- Decrease dyspnea by decreasing ventilation with exercise.
- Direct central effect on dyspnea apart from its effect on ventilation, improved ventilatory muscle function, left ventricular contractility, and pulmonary artery pressure.
- The amount of oxygen should be titrated to prevent desaturation below 90%, although even higher amounts may be advantageous for preventing dyspnea and improving exercise performance.
Pulmonary Rehabilitation

- Best studied formally in obstructive lung disease (but theoretically of use in other conditions), the key concepts are modifying behavior both to avoid a vicious cycle of deconditioning and to encourage energy-saving.

Oxford University Press, 2006; 137-155
Experience of dyspnea is affected by many factors, including education, cultural background, knowledge, emotional state, bodily preoccupation, and prior experience.

Cognitive behavioural therapy → role
## Drugs

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Respiratory depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decreased sensitivity to chemoreceptors</td>
</tr>
<tr>
<td></td>
<td>Effrent refferent dissociation</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Palliative care</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Improve diaphragm function</td>
</tr>
</tbody>
</table>