Ch. 12: Respiratory Physiology

Objectives:

1. Review respiratory anatomy.
2. Understand mechanics of breathing, gas pressure vocabulary, and the principles of surface tension, compliance, and recoil.
3. Respiratory disorders and spirometry
4. How gas exchange occurs between the alveoli & pulmonary vessels, and between capillaries & tissue.
5. Regulation of breathing (voluntary vs involuntary)
6. Hemoglobin & hemoglobin disorders

1. Respiratory Anatomy - REVIEW

2 Zones of Respiratory System:
1) Conduction zone, 2) Respiratory zone

1) Conduction Zone = from oral/nasal cavities to:

- Pharynx (throat)
- Larynx (voice box)
- Trachea
- Primary Bronchi
- Secondary Bronchi
- Tertiary Bronchi
- terminal bronchioles
Functions of Conducting Zone:

- Transports air to the lungs.
- Warms, humidifies, filters, and cleans the air.
  - **Mucus** traps small particles, and **cilia** move it away from the lungs. **Expectoration** = coughing up the mucus & debris.
- Voice production in the **larynx** as air passes over the **vocal folds**

**Structures in the larynx**

- **Glottis** – opening between vocal cords
- **Epiglottis** – closes upon swallowing to prevent food from entering airway
2) Respiratory zone

Respiratory bronchioles = smallest bronchioles, branch from tertiary bronchioles.

Alveolar sacs = honey-comb shaped, 1-cell thick sacs for gas exchange.

[~300 mill in lungs! ~760 sq ft area!]

How gases are exchanged w/blood

Surrounded by arterial & venous capillaries ("capillary plexus") for gas exchange between alveoli & blood.

QUESTIONS:

- Is this a pulmonary artery or vein?

QUESTIONS:

- Is this a pulmonary artery or vein?
Gas exchange occurs at the Alveoli
- thin cellular walls covered with capillary networks
- **300 million sacs**! - very large surface area
  - surfactant keeps the alveoli inflated

2 Types Alveolar Cells:

**Type 1 Alveolar Cells** = Make up wall of the alveolar sacs.  
It’s 97% of total lung surface area where most gas exchange occurs.

**Type 2 Alveolar Cells** - secrete **surfactant**

**Surfactant** = substance that decreases surface tension caused by water layer lining alveolar sacs.

So when you exhale and alveolar sac shrinks, the walls don’t stick together, causing collapsed alveoli (collapsed lungs!).
**Why is surfactant important?**

**Non-obstructive Atelectasis =**
Not enough surfactant to prevent alveolar sacs from collapsing when you exhale.

Leads to collapsed lungs.

**Obstructive Atelectasis =**
A foreign object blocks bronchiole, leading to alveolar sacs collapsing.

Leads to collapsed lungs.

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**Surfactants ↓ intra-alveolar pressure & prevent collapse**

**Infant Respiratory Distress Syndrome (IRDS)**

- Surfactant is produced > 28 weeks (7-8 months)

- Babies are born < 28 wks - not enough surfactant. High surface tension inside alveoli, results in collapsed alveoli, which collapses lung (non-obstructive atelectasis)

- Tx = synthetic surfactant delivered into baby’s lungs & mechanical ventilator until Type 2 alveolar cells can make surfactant.

**Acute Respiratory Distress Syndrome (ARDS)**

- Due to inflammation from infection (septic shock)
- Results in protein (serum) secretion in lungs.
- Fluid dilutes surfactant, ↑ surface tension, alveoli collapse.
- could cause lung collapse (non-obstructive atelectasis)
Coronavirus and ARDS

• Alveolar sac walls are very thin to allow for easy gas exchange.

• Chronic inflammation of any kind, which can occur with COVID-19, leads to thickening of the alveolar walls, making gas exchange difficult. (A patient with ARDS will have low oxygen levels – lower than the normal of 95% oxygen saturation of their arterial blood.)

• The inflammation also causes serum buildup within the alveolar sacs, which further decreases gas exchange.

• The fluid within the alveoli of the lungs is prone to bacterial infection. This is called pneumonia.

Radiograph of healthy lungs

The black areas show air spaces. A normal x-ray of the lungs looks like this. There should be no white spots.
Radiograph of lungs with pneumonia

The arrow points to white spots, which are fluid pockets within the alveolar sacs that have become infected with bacteria.

Thoracic cavity: Anatomy REVIEW!

Membranes of the lungs:

**Visceral pleura** = membrane covering the lungs.

**Parietal pleura** = membrane lining the pleural cavity containing each lung.
- *Parietal pleura held tight against thoracic wall by surface tension of water layer.*
- *As thoracic cage changes volume (w/ breathing) so do the lungs.*

**Intrapleural space** = empty space between the 2 pleura.
- *The 2 pleura pressed together w/serous fluid between them.*
2. Mechanics of Respiration

1) Air moves from high to low pressure
- Atmospheric air pressure = constant (760 mmHg)
- Lung air pressure depends on volume of thoracic cavity

2) Air pressure in lungs (closed chamber) changes with volume of chamber
   “Boyle’s Law” = as volume of closed chamber ↑, air pressure within ↓
   as volume of closed chamber ↓, air pressure within ↑

   Translates to lung volume & air pressure within lungs (“intrapulmonary pressure”)
   When diaphragm contracts, thoracic volume ↑, lung volume ↑, & intrapulmonary pressure ↓
   When diaphragm relax, thoracic volume ↓, lung volume ↓, & intrapulmonary pressure ↑

Boyle’s Law

Chamber volume larger
BUT air pressure lower

Chamber volume smaller
BUT air pressure higher
Diaphragm contracts, lung volume ↑, intrapulmonary pressure ↓

Diaphragm relaxes, lung volume ↓, intrapulmonary pressure ↑

https://imgur.com/gallery/oapLBD7/comment/619100343?nc=1

Table 16.1 | Pressure Changes in Normal, Quiet Breathing

<table>
<thead>
<tr>
<th></th>
<th>Inspiration</th>
<th>Expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapulmonary pressure (mmHg)</td>
<td>−3</td>
<td>+3</td>
</tr>
<tr>
<td>Intrapleural pressure (mmHg)</td>
<td>−6</td>
<td>−3</td>
</tr>
<tr>
<td>Transpulmonary pressure (mmHg)</td>
<td>+6</td>
<td>−6</td>
</tr>
</tbody>
</table>

Note: Pressures indicate mmHg below or above atmospheric pressure.
Gas Pressure Vocabulary:

Intrapulmonary pressure = pressure inside lungs
- During inhalation – is lower than atmospheric pressure (-3 mmHg)
- During exhalation – is above atmospheric pressure (+3 mmHg)

Intrapleural pressure = pressure between the pleural membranes due to elastic recoil (parietal pleura sticks to wall)
- During inhalation – is lower than atmospheric (-6 mmHg)
- During exhalation – is still lower atmospheric (-3 mmHg)

*** intrapleural pressure should ALWAYS be negative. If air enters this space, the lung can detach from thoracic wall, trapped air puts pressure on lung, & lung can collapse. **

Causes of a collapsed lung”

“Pneumothorax” = air enters intrapleural space (space between visceral and parietal pleura.
- Air trapped between the two pleural membranes removes the pressure gradient.

Result = can’t expand lungs to get air to enter! Lung collapses.

Click HERE for YouTube video of pneumothorax.

Treatment = chest tube. Click HERE

2nd pneumothorax YouTube video where doctors demonstrate with a set of lungs wrapped in a bag to simulate air invading the space between visceral parietal pleura. (As air escapes punctured lung, it fills the space making the bag expand and the lung collapse
**Important properties of the lungs:**

**A) Surface tension** = pressure resulting from thin film of water lining alveoli that resists their expansion. Makes alveoli want to collapse with exhalation.

**B) Compliance** = lungs expand when stretched (when thoracic volume ↑).
   - more lung compliance = greater capacity for “stretchiness”
   - less lung compliance = less capacity for “stretchiness”

**C) Elasticity/Recoil** = tendency of lungs to return to normal shape after stretching. *(I use the word recoil, because it avoids confusion with the “stretch” of compliance.)* (When thoracic volume ↓, lungs volume also ↓ parietal pleura keeps lungs “stuck” to thoracic wall).
B) Lung compliance

Factors that increase compliance:
- pulmonary “surfactants”
- emphysema

Smoking, Emphysema, and increased lung compliance

Smoking causes particles to settle into alveoli (where they never leave & cause chronic inflammation. The inflammation damages & destroys alveolar walls, leading to large air spaces within alveoli (thus emphysema is called an air trapping disease).
In a study published in the *American Journal of Respiratory and Critical Care Medicine*, the UNC scientists found that the lungs of vapers – like the lungs of smokers – have elevated levels of protease enzymes, a condition known to cause emphysema in smokers. The researchers also found that the nicotine in vaping liquids is responsible for the increase in protease enzymes.

https://808novape.org/scientists-show-how-vaping-induces-reactions-in-lungs-that-can-lead-to-disease/

**B) Lung compliance**

**Factors that decrease compliance:**
- many, many things!
- Anything that causes chronic inflammation can lead to ↓ compliance
- Chronic inflammation of the airways (*bronchitis*) can lead to
- scar tissue in lungs (*pulmonary fibrosis*),
- and narrowing of airways (*bronchoconstriction*)
For Ex. - Lung damage from smoking causes chronic bronchitis and formation of scar tissue (*pulmonary fibrosis*). Click image for YouTube video demonstrating scarring of the lungs from smoking. *(This will freak you out!)*
Review

• The respiratory system
  – The conduction & respiration zones
• Airway, lung, and thoracic cavity anatomy
• Alveoli (gas exchange, surfactant, factors that affect intra-alveolar surface tension and pressure)
• Mechanics of breathing (Boyle’s law and respiratory muscles), muscles of respiration.
• Gas pressure vocabulary, and pneumothorax,
• Important properties of the lungs
  – Surface tension, compliance, & elasticity.
  – Factors that affect these properties

3. Respiratory Disorders, & Diagnosing Them

**Respiratory Disorders**

**A Restrictive Disorder** = Lung tissue is damaged. Lungs are stiff, or respiratory muscles are weak.
  Examples: **Pulmonary fibrosis**

**Obstructive Disorder** = Lung tissue is normal, but resistance is increased (airways are narrowed)
  Examples: **Asthma**
    **COPD** (which includes emphysema & chronic bronchitis)
    **Cystic fibrosis**
Respiratory Disorders – Pulmonary Fibrosis

- **Pulmonary fibrosis** = buildup of fibrous tissue in lungs stiffens them (restrictive disorder)

**MANY CAUSES**
> Breathing in small particles that accumulate in & irritate the lungs:
  - Ex: **Silicosis** = (inhalation of fine glass, rock, or sand particles)
  
  Ex: **Anthracosis** (black lung disease) = inhalation of coal dust.

  Ex. **Mesothelioma** – breathing in asbestos.

  Ex. - Breathing in chemicals that irritate the lungs, as happens with **smoking**

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Respiratory Illnesses - Asthma

Muscles around the bronchioles are hyper-excitable

- **Obstructive disorder** due to inflammation, mucous secretion, & narrowing of airways (bronchoconstriction).

**Question:**
What drug would you give as a treatment to dilate the bronchioles?
Respiratory Illnesses — Chronic Obstructive Pulmonary Disease (COPD)

Chronic inflammation of airways alveolar tissue
- narrows airways & destroys alveolar walls
- proliferation of mucus-secreting goblet cells
- development of scar (fibrous) tissue = pulmonary fibrosis
- **Obstructive disorder** — due to mucus buildup and narrowed airways.

![Diagram of respiratory system showing trachea, bronchus, normal and narrowed bronchiole, and alveolus.]

People with pulmonary disorders frequently complain of dyspnea, which is a feeling of “shortness of breath.” The dyspnea, wheezing, and other symptoms of asthma are produced by increased resistance to airflow through the bronchioles (asthma is an obstructive pulmonary disorder, as discussed previously). The increased resistance to airflow is caused by bronchoconstriction and inflammation that may be provoked by allergic reactions (chapter 11).

Asthma may be treated on a sustained basis with glucocorticoid drugs (related to cortisol) that inhibit inflammation, thereby preventing or reducing the severity of “attacks.” New drugs (such as Singulair) that block the action of leukotrienes, a type of regulatory fatty acid (related to prostaglandins) that promote asthma, are now also available for this purpose. Acute asthma attacks are commonly treated with inhaled drugs (such as Albuterol) that stimulate the β-2-adrenergic receptors (a type of receptor for epinephrine and norepinephrine; see chapter 6) that promote dilation of the bronchioles.

Alveolar tissue is destroyed in emphysema, resulting in fewer but larger alveoli (see fig. 12.8). The loss of alveoli reduces the ability of the bronchioles to remain open during expiration, causing air trapping during expiration when the bronchioles collapse. The most common cause of emphysema is cigarette smoking, which indirectly causes different protein-digesting enzymes to destroy the lung tissue. The loss of alveoli and air trapping reduces gas exchange, so that people with emphysema have difficulty in both oxygenating the blood and eliminating carbon dioxide. Because of this, people with emphysema must often breathe from an oxygen tank.

Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation with narrowing of the airways and destruction of the alveolar walls. Included in the COPD category is emphysema and chronic obstructive bronchiolitis, which refers to fibrosis and obstruction of the bronchioles. The condition results in a faster age-related decline in the FEV, (discussed previously). COPD differs from asthma in that, unlike asthma, COPD is not reversible with the use of a bronchodilator such as Albuterol. Also unlike asthma, COPD is not helped much by inhaled glucocorticoids (drugs related to hydrocortisone). The vast majority of people with COPD are smokers, and stopping smoking once COPD has begun does not seem to stop its progression. In addition to the pulmonary problems directly caused by COPD, this condition increases the risk of pneumonia, pulmonary emboli (traveling blood clots), and heart failure. Patients with COPD may develop coronary — pulmonary hypertension with eventual failure of the right ventricle. COPD is now the fifth leading cause of death in the United States, and scientists have estimated that by 2020 it will become the third leading cause of death worldwide.
**Respiratory Illnesses - Emphysema**

Chronic destruction of alveolar tissue (walls between alveoli lost)
- reduces area for gas exchange
- alveoli expand easily, but can’t empty easily (air-trapping disorder)
- **obstructive disorder**

![Image of Emphysema](http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/17055.jpg)

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**Respiratory Illnesses - Cystic Fibrosis**

- Genetic disorder affecting Cl- channels on alveoli membrane. **Obstructive disorder**

Results in buildup of mucus within alveoli causing:
- Dilutes surfactant
- ↓ decreased functional alveolar size
- ↑ surface tension & intra-alveolar pressure
  (harder for alveoli to expand)
- ↓ with gas exchange
- Warmth & moisture (mucus) aids bacterial growth.
  (Vulnerable to **pneumonia**)

![Image of Cystic Fibrosis](http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/17055.jpg)
Respiratory Illnesses – Lung cancer
Pulmonary Function Tests

- **Spirometry**: air movement during respiration recorded on a spirogram.
  - Measures lung volumes and capacities
  - Can diagnose restrictive and obstructive lung disorders

3. Lung Volumes & Respiratory Vocabulary

**Spirometry** = clinical evaluation of pulmonary (respiratory) function, which allows diagnosis of lung disorders.
### TABLE 12.1 Terms Used to Describe Lung Volumes and Capacities

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Volumes</td>
<td>The four nonoverlapping components of the total lung capacity</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>The volume of gas inspired or expired in an unforced respiratory cycle</td>
</tr>
<tr>
<td>Inspiratory reserve volume</td>
<td>The maximum volume of gas that can be inspired during forced breathing in addition to tidal volume</td>
</tr>
<tr>
<td>Expiratory reserve volume</td>
<td>The maximum volume of gas that can be expired during forced breathing in addition to tidal volume</td>
</tr>
<tr>
<td>Residual volume</td>
<td>The volume of gas remaining in the lungs after a maximum expiration</td>
</tr>
<tr>
<td>Lung Capacities</td>
<td>Measurements that are the sum of two or more lung volumes</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>The total amount of gas in the lungs after a maximum inspiration</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>The maximum amount of gas that can be expired after a maximum inspiration</td>
</tr>
<tr>
<td>Inspiratory capacity</td>
<td>The maximum amount of gas that can be inspired after a normal tidal expiration</td>
</tr>
<tr>
<td>Functional residual capacity</td>
<td>The amount of gas remaining in the lungs after a normal tidal expiration</td>
</tr>
</tbody>
</table>

Additional Respiratory Vocabulary:

- **Apnea** = absence of breathing
- **Dyspnea** = labored or difficult breathing
- **Eupnea** = normal breathing at rest
- **Hyperventilation** = excessively rapid ventilation (will decrease alveolar CO2)
- **Hypoventilation** = low ventilation (will increase alveolar CO2)
- **Pneumothorax** = presence of gas in intrapleural space causing lung collapse
Review

• Respiratory disorders
  – Restrictive vs Obstructive
  – Pulmonary fibrosis (and its causes)
  – Asthma
  – COPD
  – Emphysema
  – Cystic fibrosis

• Testing for respiratory disorders
  – Spirometry
  – Spirometry vocabulary (IRV, ERV, TV, VC, RV, and TLC, minute ventilation)
  – Additional respiratory vocabulary (eupnea, dyspnea, apnea, hyperventilation, hypoventilation)

4. Basics of Gas Exchange at Lungs and at Body Tissues

Gas exchange between 2 structures is dependent on pressure gradient of dissolved O2 & CO2

* Gas moves from side with higher pressure (from dissolved gases) to side with lower pressure & visa versa

*Gas wants to move “downhill” from high to low pressure!
Gas exchange between lung alveoli & pulmonary vessels:

> Alveolar PO2 = 105 mmHg, higher than that in pulmonary arteries (40 mmHg)

> Alveolar PCO2 = 40 mmHg, lower than that in pulmonary arteries (46 mmHg)

Gas exchange between systemic capillaries & tissues:

> Tissue PO2 (<100 mmHg) = lower than O2-rich arterial blood (100 mmHg)

> Tissue PCO2 (>40 mmHg) = higher than that in arterial blood (40 mmHg)
Review

- Pulmonary function tests (spirometry)
- Alveolar PO$_2$ lower than atmospheric
- Gas exchange at tissues & at alveoli of lungs
  Depends on differences in partial pressures of O$_2$ and CO$_2$

Motor neurons from 3 brain areas control breathing muscles:

1) Voluntary Breathing
   = primary motor cortex of frontal cerebral lobe.

2) Involuntary Breathing =
   Medulla – respiratory center regulates respiratory rate.
   Pons  – apneustic center (stimulate inhalation)
   – pneumotaxic center (inhibit inhalation)
What happens to minute ventilation after:
• Hypoventilation?

• Hyperventilation?

Autonomic motor control breathing involves:

Chemoreceptors:

➢ Aorta & carotid artery chemoreceptors (called peripheral chemoreceptors)
  - sense blood O2 and CO2 levels

➢ Medulla chemoreceptors (called central chemoreceptors)
  - sense CSF O2 and CO2 levels
**Negative Feedback regulation of blood pH (by blood CO2 content)**

**Stimulus** = ↓ blood pH (acidosis) blood O2 is too low (CO2 is high)
**Sensors** = arterial chemoreceptors detect high CO2 in blood, Medulla senses high CO2 in CSF.
**Integrating center** = Medulla’s respiratory center
**Effectors** = respiratory muscles
   - ↑ respiratory depth & rate (↑ minute ventilation) Get rid of excess CO2
**Effect** = ↑ blood pH to normal

**Stimulus** = ↑ blood pH (alkalosis) blood O2 is too high (CO2 is too low)
**Sensors** = arterial chemoreceptors detect low CO2 in blood, Medulla senses low CO2 in CSF.
**Integrating center** = Medulla’s respiratory center
**Effectors** = respiratory muscles
   - ↓ respiratory depth & rate (↓ minute ventilation) Retain a little CO2
**Effect** = ↓ blood pH to normal

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**Normal Blood pH = 7.35 – 7.45**
**Blood pH maintained by buffering CO2 with HCO3-**

Blood with high CO2 or H+ content = acidic (acidosis)
Blood w/lower CO2 or high HCO3- content = alkaline (alkalosis)

**Blood pH (Acid/Base balance) based primarily on blood CO2 content and metabolic activities in body:**

1) **Respiratory component** = where CO2 (a volatile acid) in blood eliminated by lungs (exhalation).
   - Increased respiratory rate ↑ blood pH (respiratory alkalosis)
   - Decreased respiratory rate ↓ blood pH (respiratory acidosis)

2) **Metabolic component** = non-volatile acids in blood (i.e. lactic acid, fatty acids, ketones) eliminated by liver, kidneys, or other organs.
Acidosis = increased acids in blood (pH below 7.35)
Alkalosis = decreased acids in blood (pH above 7.45)

Respiratory acidosis = ↓ blood pH due to ↓ respiratory rate (hypoventilation) – not enough CO2 waste exhaled by lungs.

Respiratory alkalosis = ↑ blood pH due to ↑ respiratory rate (hyperventilation) – too much CO2 exhaled by lungs.

Metabolic acidosis = excess metabolic production of acids (i.e. ketosis) OR loss of bases (i.e. bicarbonate) from chronic diarrhea or kidney problems (excrete too much HCO3-)

Metabolic alkalosis = too much bicarbonate (not enough excreted by kidneys) OR loss of metabolic acids such as with chronic vomiting (lose HCL).

Review

• Regulation of breathing (voluntary vs involuntary)
  – Primary motor cortex (voluntary)
  – Medulla & Pons (involuntary)

• Acid / Base imbalance
  – Metabolic Acidosis & Alkalosis versus
  – Respiratory Acidosis & alkalosis
6. Hemoglobin & Hemoglobin Disorders

Hemoglobin =

- 4 protein chains w/ 4 iron-containing heme (pigments)
- Each heme group binds with 1 O₂ molecule
- Each RBC has ~280 million hemoglobin molecules (each RBC can carry ~billion O₂ molecules! (4 X 280 million)
- Hemoglobin bound to O₂ = “oxyhemoglobin”
  (Arterial blood 97% saturated w/ oxyhemoglobin = bright red)
- Hemoglobin lacking O₂ = “deoxyhemoglobin”
  (venous blood dull red or maroon)

Hemoglobin Disorders:

Carbon Monoxide = odorless, color-less gas that binds w/ hemoglobin to create carboxyhemoglobin in RBCs.

Carboxyhemoglobin has lower affinity for O₂.

Result:
> Hypoxia (called carboxyhemoglobinemia)
> Death
Methemoglobinemia = disorder in which hemoglobin’s iron (a component of heme) is “ferric” rather than “ferrous”.
> this hemoglobin called methemoglobin (pronounce as “met-hemoglobin”)
> Methemoglobin has ↓ ability to release (unload) O2 at tissues.
> Tissues chronically O2-starved.
> Patients are hypoxic & BLUE!

“Blue baby syndrome” = babies turn blue (hypoxia) from drinking milk made w/nitrate contaminated water. Nitrate causes formation of methemoglobin.
Neonatal jaundice At birth switch from hemoglobin-F (fetal) to hemoglobin-A (adult)
- Body removes RBCs with hemoglobin f.
- Liver removes biliruben from destroyed hemoglobin f.
- Liver sometimes not mature enough to remove biliruben.
- Biliruben builds up.
- Baby turns yellow. (happens in up to 50% newborns)

Treatment:
Sickle Cell Anemia = homozygous recessive condition in which body produces RBCs with hemoglobin-S rather than hemoglobin-A.
- Hemoglobin-S turns RBCs into sickle-shape.
- Sickled RBCs carry less O2 (cause hypoxia)
- Sickled RBCs tend to form clots (thrombus)
- Patients more prone to embolism.
- More prone to ischemic events.

Hemoglobin Disorders contin...

Review

- Regulation of breathing
  – Medulla & pons
- Chemoreceptors
  – central, peripheral
- Hemoglobin O₂ transport:
  – Oxyhemoglobin & deoxyhemoglobin
  – Abnormal hemoglobin (carboxyhemoglobin, methemoglobin)
  – Neonatal jaundice
  – Sickle cell