CHAPTER 1

Cellular Respiration and Diffusion

INTRODUCTION

Breathing in and out is key to staying alive. It's so important that even when we forget to breathe, our nervous system picks up the slack and keeps going. The process of breathing provides oxygen and removes carbon dioxide from the body. This process is essential to sustaining each and every cellular task within our bodies. The focus of this book is how the body achieves this seemingly simple process. We will take you from a single cell and how it regulates oxygen and carbon dioxide to the large-scale gas transport and delivery in the body under normal and pathologic conditions. So, sit back, relax, and take a deep breath!

If indeed you take a breath right now, you will breathe in air. Air in the atmosphere is a simply a mixture of gases. Atmospheric air, as it exists today, consists of about 21% oxygen, 78% nitrogen, 0.04% carbon dioxide, and some other miscellaneous gases such as argon. (Carbon dioxide makes up so little of the atmospheric air that it even gets beat out by argon, which weighs in at 1%. Seriously!)

But it wasn't always this way. In fact, over 2.5 billion years ago, things weren't looking too good for our oxygen-loving brethren. There was almost no oxygen in the atmosphere, and there was very little food around. So, some opportunistic little buggers called cyanobacteria took the warmth of the sun and made sustainable energy out it, much like plants do today. In the process they gave off oxygen as "waste."

Little by little cyanobacteria began filling up the oceans with oxygen. The dissolved oxygen began to diffuse throughout the water (hopefully you'll remember the principles of diffusion from our last book "Back to Basics in Physiology: Fluids in the Cardiovascular and Renal Systems"), and as the oceans filled with this "waste product" it diffused into the atmosphere. Over the next two billion years, the concentration of oxygen in the air reached the 21% we know and enjoy today.

Back to Basics in Physiology. DOI: http://dx.doi.org/10.1016/B978-0-12-801768-5.00001-0

As oxygen became more and more plentiful in the environment, creatures began using this oxygen to create energy from available food sources more efficiently, and were able to grow larger than their non-oxygen-consuming counterparts. With size came more food consumption and a greater need for mobility, and with mobility and size came more energy utilization. Over time, organisms migrated from the water to land. Cyanobacteria made room for plants in the sea and on land, which produced even more oxygen. As organisms developed ways to use this newfound energy (e.g., growing brains!), they developed a larger need for oxygen, produced more carbon dioxide, and along the way came up with some pretty ingenious mechanisms to ensure *constant* oxygen delivery and carbon dioxide removal.

In our bodies today, out of the millions of functions that need to be carried out minute by minute in order to allow for life to proceed "uneventfully," oxygen (O_2) and carbon dioxide (CO_2) exchange are arguably two of the most important processes our bodies require to stay alive. If the human body is deprived of oxygen, it will die far quicker than if deprived of food or water. If someone removed your kidneys right now, you would live for potentially several days. If they removed your heart or your lungs, the main organs responsible for moving the oxygen and carbon dioxide around the body, you would die within minutes. In fact, doctors' primary goals in the setting of any medical emergency always revolve around bringing back or "stabilizing" a patient's oxygen delivery, and to a lesser extent, carbon dioxide clearance. In fact, the classic ABCs of patient care (what doctors need to worry about first!) stand for Airway, Breathing, and Circulation. But why exactly are these two items so important?

O_2 is consumed and CO_2 is produced by all living cells in the body every second of every day in a process called aerobic cellular respiration. This process is absolutely vital to creating the energy that keeps the cells alive. O_2 and CO_2 allow for the most efficient energy extraction from the food we eat. In order to keep creating energy, these cells need a system that will move new O_2 in and take CO_2 out. So, before we go on to understand exactly how O_2 and CO_2 move in and out of the body, we need to take a step "in" and first understand why O_2 and CO_2 are important, and how they help create energy at the cellular level. Then we can move on to how these vital gases get in and out of cells and why blood is specialized to help aid this process. In the subsequent chapters, we will apply these concepts to the lungs and the rest of the cardiovascular system. By understanding how O_2 and CO_2 are used and how they move, the form and function of the rest of the pulmonary and cardiovascular systems will make sense intuitively.

Key

O_2 is consumed and CO_2 is produced in the creation of energy.

O_2 AND CO_2 FOR ONE CELL: MECHANICS OF SINGLE CELL GAS EXCHANGE

A cell is the most basic unit of life (ignoring viruses, which are a bit of a gray area). As such, it needs to be able to grow and respond to threats in its environment long enough to reproduce before eventually dying. Biochemically speaking, this involves a myriad of complex tasks. However, in order to perform all of these incredibly complex tasks, one thing is key: energy! Energy is needed for every major process the cell undertakes: movement of ions, signaling, and reproduction. We need energy for everything. But where does this energy come from?

Role of Oxygen (O_2) and ATP

Much like how money is used to allow us to survive in a modern economy, cells must have a form of "energy currency" that allows them to rapidly generate and store energy that can be used at a moment's notice. In organisms, this energy is most commonly stored as ATP, or adenosine triphosphate. Adenosine is a nucleoside. Nucleosides (a nitrogenous base with a carbohydrate backbone) are some of the most ubiquitous chemical compounds found in life. They are the building blocks of DNA and RNA, so your body has loads of them on hand. If multiple phosphate molecules are added to them, they become increasingly energy rich. *In short, it is energy in the form of ATP that fuels life.* As we shall soon see, oxygen makes ATP formation a heck of a lot more efficient. And efficient is good!

Generally speaking, ATP can be made without the help of oxygen. Many microorganisms from many walks of life live in some of the most hostile and oxygen-poor environments on this earth, but they can still thrive. They need to worry about providing fuel for only *one* little cell, though. The human body, on the other hand, is made up of *trillions* of cells, and within it ATP is broken down and formed and broken down and formed over and over again, millions of times a day. This pathway is so active that the body effectively turns over its own body weight in ATP every day! You can imagine then that ATP production can become exceedingly expensive to produce. Thankfully, oxygen helps us make ATP creation a lot easier.

Let's look at ATP fabrication and recycling a little bit more closely, shall we? As we just mentioned, oxygen allows for the efficient creation of energy in the form of ATP. In more general terms, energy is extracted from the food we eat. As such one of the key molecules in all the food we eat is glucose. The process through which oxygen is used to extract energy to make ATP from glucose is called cellular respiration (Figure 1.1):

$$\text{Glucose} + O_2 \rightarrow CO_2 + H_2O + \text{ATP}$$

Key

O_2 is consumed and CO_2 is produced during aerobic respiration. The product is energy!

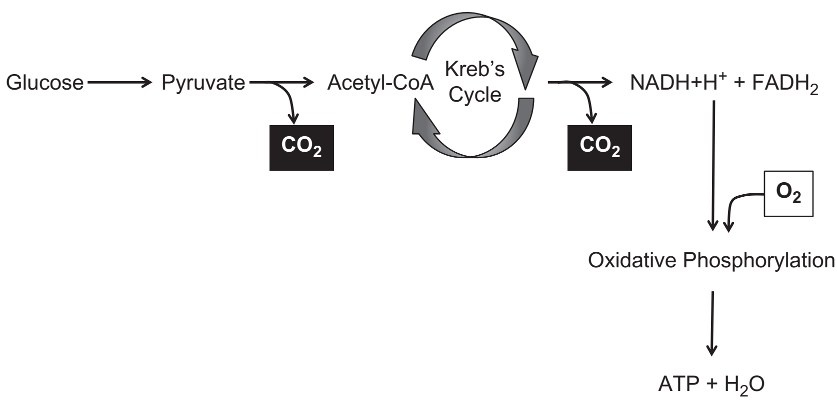

Figure 1.1 Aerobic cellular respiration is the process through which cells use glucose and oxygen to produce ATP and H_2O, with CO_2 as a byproduct of the biochemical reactions.

> ### Clinical Correlate
>
> **Ischemia**
>
> Ischemia is what happens when cells suddenly are unable to receive oxygen and get rid of carbon dioxide. Specifically, the term is used to describe a loss of blood flow. As we'll see in later chapters, one of the main functions of blood is to deliver O_2 to tissues and remove carbon dioxide. When there is no blood flow, there is no O_2 delivery, and there is no CO_2 removal. Therefore, cells are no longer able to produce energy, and they begin to malfunction. One of the best examples of this is myocardial ischemia—a heart attack. When blood flow to a portion of the heart muscle stops, the heart muscle cells can't make energy. This causes inflammation and abnormal functioning of these cells. Common clinical manifestations of a myocardial infarction are pain and arrhythmias arising from the infarcted tissue.

Role of Carbon Dioxide (CO_2)

The amount of CO_2 that is in the air we breathe is relatively low, but inside the body the amount of CO_2 is much, much higher. As O_2 is actively being consumed during cellular respiration, CO_2 is being produced as a byproduct of the same biochemical pathway (Figure 1.1). Remember: While O_2 is being consumed, CO_2 is being produced. Similar to what happens with O_2, the production of CO_2 by the cell is closely linked to metabolism; the higher the metabolic rate, the more CO_2 produced. The major goal of metabolizing food is to break down the food into its simplest chemical form (usually glucose) and then to remove hydrogen ions and electrons from it. The removal of hydrogen ions and electrons will ultimately power an enzyme called ATP synthase. This enzyme creates ATP, and in doing so creates usable energy. There are many biochemical reactions involving the removal of hydrogen ions and electrons from food, and they differ depending on whether the food is a sugar, a protein, or a fat. Some of these reactions, called decarboxylation reactions, result in the removal of a carbon atom, and it is from these reactions that CO_2 is generated.

CO_2 is not a useless byproduct of metabolism though; it has an extremely important role in the body as an acid base buffer, as we will see in further chapters. For now, suffice it to say that any excess accumulation of CO_2 within the cell is unwanted and could disrupt adequate cellular functioning; therefore, CO_2 must be continuously shuttled outside of the cell.

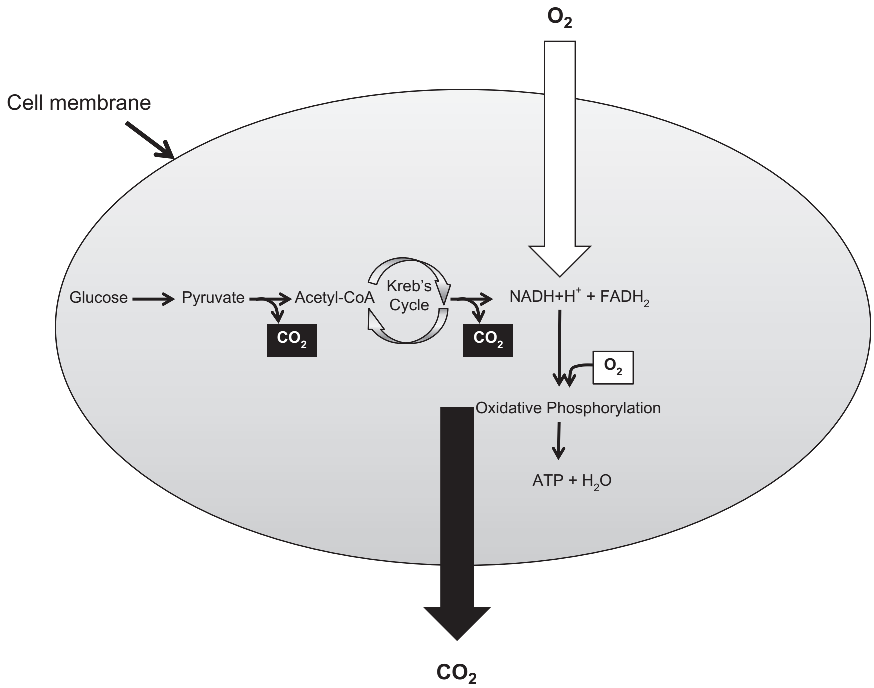

Figure 1.2 In a single cell, O_2 moves from the outside of the cell to the inside (white arrow), while CO_2 moves from the inside to the outside of the cell (black arrow).

Single Cell Exchange Requirements

We've established that during the aerobic production of ATP, O_2 is consumed and CO_2 is produced by the cell (Figure 1.2). Because O_2 gets consumed by the cell, it must first be brought to the cell from the outside, while CO_2 is produced and must be shuttled from inside to outside in order to prevent a toxic accumulation of CO_2 inside the cell. But how do these gases move across the cell membrane? Unlike ions, which require proteins to be shuttled in and out of the cell due to a lack of permeability, gases can freely diffuse in and out of the cell. Because gases are freely diffusible, the only thing that regulates the movement of O_2 and CO_2 across the membrane is the pressure difference between both sides of a membrane and the solubility of the gas. Therefore in order to fully understand the movement of gases between cells and in the body, a brief review of the basic principles regulating the behavior of gases in the environment is warranted.

REVIEW OF THE PHYSICAL PROPERTIES OF GASES

The physical and chemical properties that guide the diffusion of gases are far too complex to be entirely reviewed in this book. However, we will highlight the bare minimum that we believe is essential to understanding the movement of O_2 and CO_2 in the body. With that in mind, let us push forward!

There are four fundamental states of matter: solid, liquid, gas, and plasma. A simple way to define the differences in the states of matter is to think of the kinetic energy of their molecules. All molecules move constantly, and this movement has the capacity to do work. Kinetic energy is the energy that that these molecules possess due to the movement of their molecules. The more kinetic energy, the more they're going to move. Solids have the least amount of kinetic energy and plasma has the highest amount of kinetic energy. As the kinetic energy increases, molecule movement increases. Sugar-laden 4-year-olds running wild at a birthday party = high kinetic energy; the same 4-year-olds asleep after the sugar crash = low kinetic energy. As kinetic energy increases in the molecules that make up a given compound, it becomes harder for the compound to keep its shape as the intermolecular bonds weaken from all the motion. The more kinetic energy the molecules have, the more space they will occupy and the less likely they are to interact. Solids are solids because of the stable interactions between molecules. Gases have a much higher amount of kinetic energy; this means that gas molecules moving around all over the place take up a lot more space. (Keeping with our young child analogy, a sleeping child equaling low kinetic energy does not occupy that much space. A sugar-crazed toddler running around the house can feel as if no place is big enough to contain him or her.) Thinking of the matter in this way (and specifically, gases) leads us to the following point. There are four basic physical properties that significantly impact the behavior of gases by impacting their molecular kinetic energy in a manner of speaking:

- Number of particles
- Temperature
- Volume
- Pressure

Key

The key determinants of the behavior of a gas are the number of particles, its temperature, its volume, and its pressure.

Of these factors let's take a closer look at pressure, since this will become relevant when we discuss gas movement in the body. What exactly is pressure? Pressure is the amount of force that is applied by a particular compound in a given area. If that compound were a gas, it would be the force from all those collective collisions banging up against the sides of, say, a container holding said gas:

$$\text{Pressure} = \frac{\text{Force}}{\text{Area}}$$

Pressure is therefore a function of the strength between the collisions of the molecules in the gas and the amount of space these molecules have to move around in. So how exactly do we quantify pressure? There are various units that can be used: atmospheres (ATM), Pascals, pounds per square inch (PSI), Torr, among others. We will be using two particular units: millimeters of mercury (mmHg) and centimeters of water (cmH_2O). Both of these methods work in a similar fashion (Figure 1.3). A graduated glass column is filled with either mercury (Hg) or water (H_2O), and it's connected through an adaptor to wherever you want to

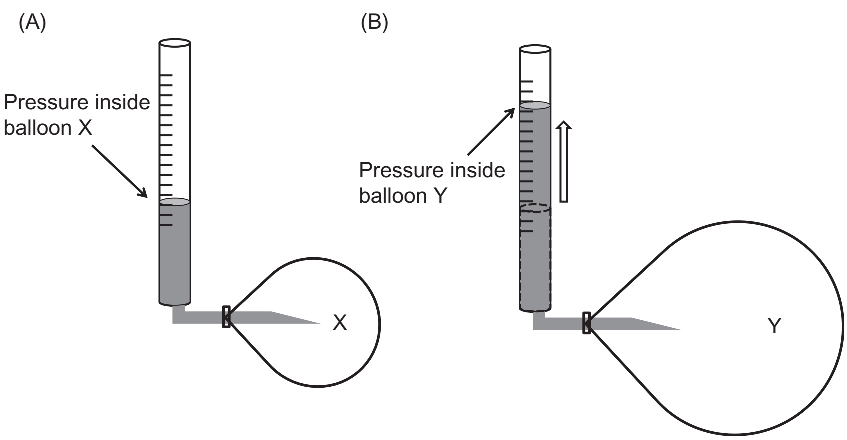

Figure 1.3 Displacement of a column of fluid (grey) allows for the measurement of pressures. (A) Low pressures only make the column of fluid rise slightly. (B) Higher pressure makes the column of fluid rise higher. The pressure, in either mmHg or cmH_2O, is the total amount of displacement measured in the column.

measure the pressure. The pressure inside the place of interest will displace the water or mercury a specific distance either up (high pressure) or down (low pressure). In the case of mercury this is measured in millimeters and in the case of water it is measured in centimeters. The amount of fluid that ends up getting displaced is measured. It's typically much easier to see a liquid than a gas, so this form of measurement has been historically convenient. Given that mercury has a greater density than water, mmHg are used for higher pressures (it is harder to displace a dense liquid so we need higher pressures), and cmH_2O are used for lower pressures (easier to displace a less dense liquid with a lower pressure). So whenever we mention mmHg or cmH_2O, what we are referring to is how much pressure is in a particular space. There are several pressures that we are required to memorize: first is the atmospheric pressure at sea level. This is the standard pressure of air at sea level, which is 760 mmHg. All further calculations in the book will be based on sea level atmospheric pressure!

Another concept that requires a brief mention (we'll touch on it again in Chapter 2) is that of partial pressures. We mentioned that the pressure of air at sea level is 760 mmHg. But air is simply a collection of gases! If we're thinking of these molecules as individuals, each with their own weight (oxygen, e.g., is heavier than nitrogen) and their own size (nitrogen, due to different electron configuration is actually larger than oxygen), then we can imagine that each individual gas collectively exerts its own pressure within the air! Thus, a partial pressure is simply the amount of pressure that an individual gas within a mixture exerts. For example, we said earlier that O_2 makes up 21% of atmospheric air, but this tells us the relative amount. Without knowing the total pressure, this number doesn't help us exactly. We want to know the amount of oxygen in absolute terms (e.g., its partial pressure in mmHg). At sea level, where we know that the total air pressure of the atmosphere is 760 mmHg, we can determine that 21% of this is 160 mmHg. This would be the value of the partial pressure of oxygen within the atmosphere at sea level. If we were to hypothetically increase the percentage of oxygen to 40%, but keep the total atmospheric air pressure the same, the partial pressure of O_2 would increase from 160 mmHg to 304 mmHg. Conversely, if we were to move much higher up away from sea level, where there is less gravitational force acting on molecules and a lower total air pressure (let's say 500 mmHg instead of 760 mmHg), the fraction of inspired O_2 (FiO_2) will remain the same at 21%, but the ABSOLUTE pressure of O_2 will decrease from 160 mmHg to 105 mmHg. Therefore it is important to consider both the total pressure and the fractional percentage that each gas we're studying represents.

REVIEW OF DIFFUSION AND GRADIENTS

In its simplest terms, diffusion is the movement of substance X from an area where there is a lot of X to an area where there is not that much X. When discussing gases, we can talk about a gradient from an area of high pressure to an area of low pressure along the pressure gradient (Figure 1.4). In our previous book, *Back to Basics in Physiology: Fluids in the Cardiovascular and Renal Systems*, we had defined diffusion as the movement of substance X using the term concentration rather than pressure. This was the case because we were talking mainly about solutes and solvents. Since now we are referring to gases we talk in terms of pressure. Other than pressure, the factors that modify the diffusion across a semipermeable membrane of any one substance in particular can be summarized with the following formula:

$$\text{Diffusion } \alpha \frac{\Delta P \times SA \times sol}{dist \times \sqrt{MW}}$$

where:

> $\mathbf{\Delta P = (P_1 - P_2)}$. The difference in pressures between compartment 1 (P_1) and compartment 2 (P_2). As you can see this is in the numerator; thus, the greater the pressure difference the greater the diffusion that will take place.

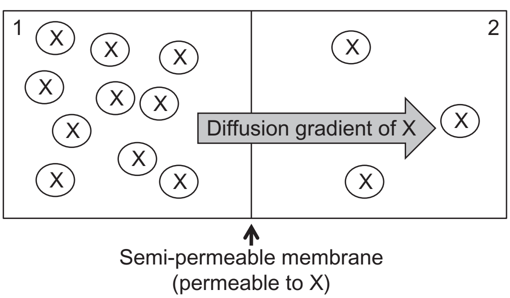

Figure 1.4 Diffusion of X from compartment 1 to compartment 2 follows the gradient that exists between A (high pressure) and B (low pressure).

SA = Surface area. How much membrane space is available for difusion to occur. Again, numerator. The more membrane through which exchange can occur, the more diffusion will take place.
sol = Solubility. Determined by two things: (1) the semipermeable membrane (e.g., if something is not soluble to the membrane it will never diffuse across no matter the pressure difference or surface area) and (2) the states of matter on either side of the membrane (e.g., is it diffusing from gas to gas? Liquid to gas? Gas to liquid?). We will approach this particular concept again in the upcoming chapters, but for now let us cover the highlights. When diffusion of gases is occurring solely as gases and does not involve liquids, the only impediment to diffusion will be how permeable the membrane is to a particular gas (Figure 1.5A). In contrast, when a gas is diffusing from a gas to a liquid (Figure 1.5B), conditions change. The gas must first dissolve in the liquid before it can diffuse throughout the liquid. This is when solubility becomes even more important, because how readily a gas will dissolve (e.g., in water) will have a large impact on its rate of diffusion. (This explanation applies to any fluid, but considering that water will be the basis of our discussions, we will continue to discuss solubility of gases in water.)
dist = Distance. How much distance is there from one compartment to another? As the distance increases, diffusion decreases (in this case this variable is in the denominator). This is especially

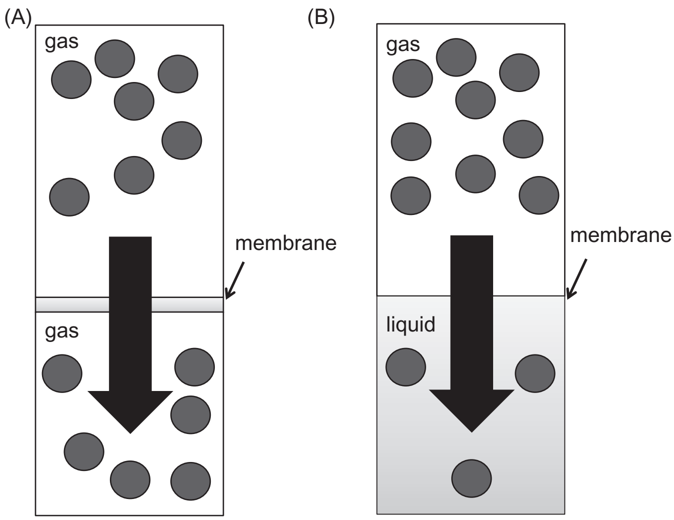

Figure 1.5 The solubility of a gas in a particular liquid will determine its diffusion into and through the liquid.

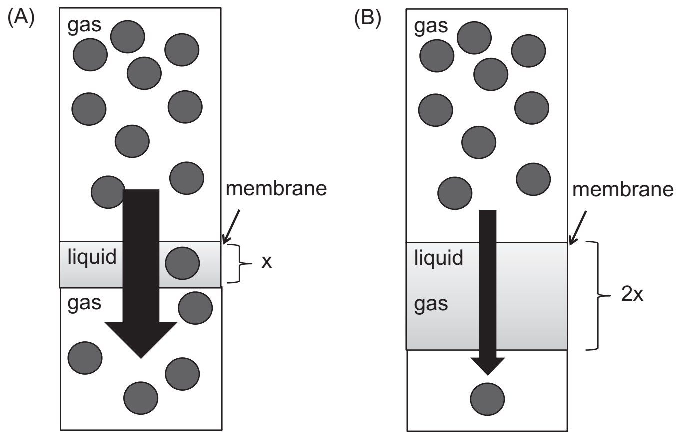

Figure 1.6 Distance is one of the key determinants of diffusion. As distance increases (gray area), diffusion decreases (black arrows). The converse is also true, as the distance decreases, diffusion increases.

important in certain clinical conditions, which we will approach later in the book. But for now, consider Figure 1.5; the liquid membrane dividing both compartments has a predefined distance (x) (Figure 1.6A), and as this distance doubles (Figure 1.6B), diffusion decreases. If distance were to decrease, diffusion would increase proportionally.

MW = Molecular weight. MW of the substance we're analyzing. Stated differently, how big is the molecule that is going to diffuse? The bigger the molecule, the less easily it will diffuse.

These five factors determine diffusion across a semipermeable membrane. We can further classify them into two groups (Figure 1.7):

1. Factors that favor diffusion; that is, as they increase, diffusion increases as well:
   - ΔP
   - Surface Area
   - Solubility
2. Factors that oppose diffusion; that is, as they increase, diffusion decreases:
   - Distance

A simplified version of this formula is:

$$\text{Diffusion}\ \alpha \frac{\Delta P \times SA}{dist}$$

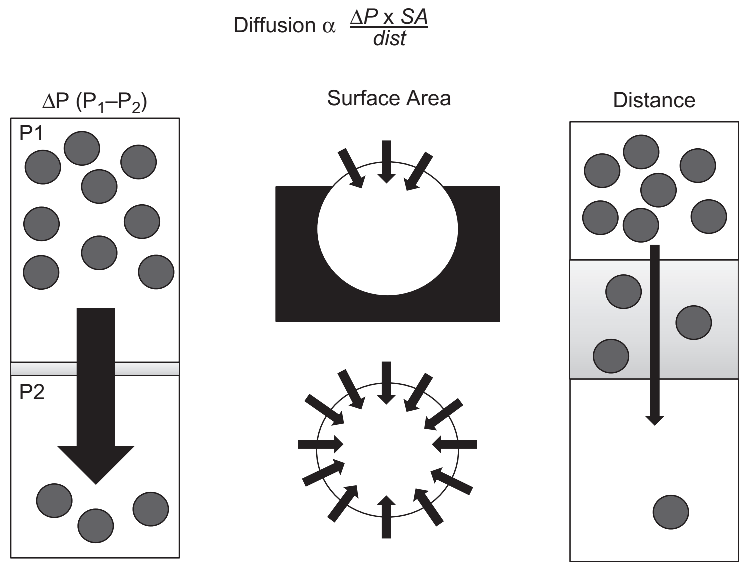

Figure 1.7 The formula for diffusion has two nonvariable factors: solubility (sol) and MW (molecular weight). These are intrinsic to each substance and can't be readily altered. From the remaining three variables, two favor diffusion (ΔP, and surface area) and one opposes diffusion (distance). From this image we can see that as ΔP or surface area increases, diffusion (black arrows) increases. However if distance increases, diffusion decreases.

In this simplified version, we have eliminated solubility and molecular weight. This is because solubility can't be easily altered. In fact, in the body the solubility of different gases is relatively fixed. Therefore it's not going to be a variable that affects diffusion in a significant way under steady state conditions (although we will see that it does explain some of the differences we see later between oxygen and carbon dioxide!). Additionally for simplification we will not include MW since it isn't exactly something we can modify.

Key

As ΔP and surface area increase, diffusion increases. As distance increases, diffusion decreases.

This formula explains diffusion throughout the entire body and for every system. This means that if you understand this formula you will be able to understand the pathophysiological mechanism of diffusion problems everywhere in the body.

Clinical Correlate

Pathologic Alterations in Diffusion

In many diseases that impair adequate gas exchange, ultimately what is altered is one of the parameters of our simplified diffusion formula. For example, pneumonia can fill the lung with inflammatory cells and fluid can have a significant decrease in the surface area and the ΔP, and potentially if the pneumonia is very severe, an increase in the distance through which gases have to diffuse! This is why patients with pneumonia can present with difficulty exchanging O_2 and CO_2. Likewise patients with Chronic Obstructive Pulmonary Disease (COPD) can have decreases in surface area and increased distance, which lead to poor O_2 and CO_2 exchange. Once we understand the root cause of the disease, we can try to orient our treatment to reestablish normal function of the lungs.

DIFFUSION AND THE CELL

After our brief review of diffusion, let's go back to discussing our single cell example from the previous paragraphs. As we mentioned previously, cells in the body consume O_2 and produce CO_2. This is happening in each and every cell. Each single cell is consuming O_2 and therefore, O_2 must diffuse through the cell wall from the outside in. Along the same lines, CO_2 is being produced and it must diffuse from the inside of the cell to the outside. Consider our simplified diffusion formula:

$$\text{Diffusion } \alpha \frac{\Delta P \times SA}{dist}$$

If we're talking about a single cell, surface area is going to be more than adequate to allow for both diffusion of O_2 and CO_2 and the distance; that is, the width of a single cell membrane is not a huge obstacle to diffusion, therefore the most important factor determining the diffusion of O_2 and CO_2 in this example is the ΔP (Figure 1.8).

For O_2:

- $\mathbf{\Delta P = (P_1 - P_2)}$. P_1 is outside the cell, and P_2 is inside the cell. Given that O_2 is being consumed inside the cell, we can automatically assume that the pressure of O_2 inside the cell is going to be lower than the pressure of O_2 outside. Therefore, if P_2 is less than P_1, an

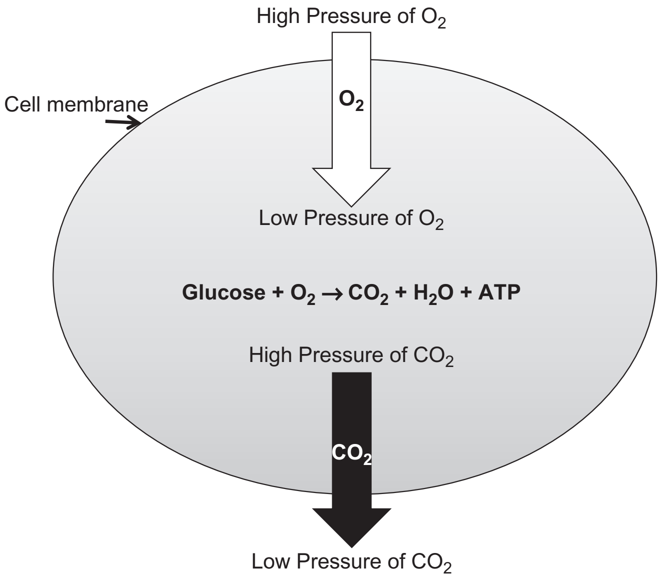

Figure 1.8 The diffusion of O_2 and CO_2 across the cell membrane follows their individual pressure gradients (see arrows).

O_2 gradient is generated from the outside of the cell toward the inside. This means that O_2 will tend to diffuse toward the inside of the cell.

For CO_2:

- $\mathbf{\Delta P = (P_1 - P_2)}$. P_1 is inside the cell, and P_2 is outside the cell. The situation is reversed in this case. CO_2 is being produced; therefore, we can automatically assume that the pressure of CO_2 inside the cell is higher than outside the cell. This generates a favorable CO_2 diffusion gradient from the inside to the outside of the cell.

If we take all of these considerations into account, in the case of the single cell we can say that the requirements of O_2 consumption and CO_2 excretion are easily met. However, more complex organisms are made up of an increasing number of cells, and as the number of cells increased, so did the metabolic requirements. Unfortunately, what did not increase was the surface area! That meant organisms had to develop a way of increasing the surface area that's available for exchange while maintaining structural integrity.

DEVELOPMENT OF MULTICELLULAR ORGANISMS FROM SINGLE CELLS, O_2 AND CO_2 FOR TRILLIONS OF CELLS

Simple diffusion might be all that was needed if organisms never evolved beyond a few individual cells floating in a sea. However, as you know, organisms have evolved since then. As they made the jump from unicellular to multicellular, they did so at the expense of surface area! As organisms evolved, cells became larger, individually consumed more energy, and of course collectively consumed a great deal more energy than their single-celled counterparts. This presented a *huge* engineering problem! There were increasing metabolic demands for O_2, and an increased production of CO_2, but at the same time the surface area available for gas exchange with the outside environment was decreasing. The bigger an organism grew, the farther away from the atmosphere its inner cells became. The more the distance increased between the cells and the environment, the more difficult it became to oxygenate them. So, how do you feed all those hungry cells with oxygen? And how do you clear out all the waste products when so many cells are so far away from their external environment? Thankfully, nature developed a solution: specialized labor.

Any student of nature can guess that there are probably some advantages to being multicellular from an evolutionary standpoint, no? The most obvious one that comes to mind is specialization of labor. If you're a single cell, you have to be a jack-of-all-trades and a master of none. But if you're a multicellular organism, then you can have cells that specialize and spend their entire existence devoted to just one task. You can create cells that specialize in sensing your environment (eyes, ears, nose, tongue); cells that protect you from said environment (skin, immune system); cells that help you get around your environment with locomotion (skeleton, muscles); cells that absorb food (digestive system); cells that keep all these systems organized and communicating together (nervous system, endocrine system). But most vitally important (pun intended) would be the cells whose job is to make sure that all of these specialized cells have enough energy to do all of these things; cells that help supply the rest of the cells in our body with O_2 and help rid the body of excess CO_2. And these are the cells that make up the respiratory system, cardiovascular system, and blood.

In the next chapter, we're going to look at how the body engineered a solution to this problem: how to deliver oxygen from the atmosphere to the cell, and how to deliver carbon dioxide from the cell to the atmosphere. As we'll see, rather than trying to reinvent the wheel, the body relies on diffusion to do most of the work. At every level of the body, diffusion is what drives gas exchange. Whether it's through creating a larger gradient, maximizing surface area, or minimizing the distance oxygen and carbon dioxide need to travel, the body engineered a system where diffusion does most of the work. It will become apparent in subsequent chapters that the lungs, heart, blood vessels, and blood all work in symphony to make sure that a healthy gradient from the atmosphere to the cell is always maintained. They make sure that there is as much surface area as possible through which oxygen and carbon dioxide can diffuse, and they make sure that there is as little a distance over which it needs to take place. They simply serve to get the gases *close* to where they need to go, and they let diffusion do the rest. This is a recurrent theme throughout the body, and thus will be a recurrent theme throughout this book.

Key

Diffusion is what drives gas exchange to the trillions of cells within the body. Fresh gradients, large surface area, and short distance is how the body keeps oxygen flowing in and carbon dioxide flowing out.

CLINICAL VIGNETTES

A 56-year-old stockbroker with a 20-pack/year history of smoking and untreated hypertension presents to the emergency department complaining of 10/10 chest pain that started suddenly approximately 45 minutes ago while he was at work. The pain is "crushing" and radiates to his left arm. He is short of breath, and feels light-headed. An EKG is performed, which shows a clear S-T segment elevation in leads V4−V6, consistent with the diagnosis of left heart wall myocardial infarction (a heart attack).

1. Why does this patient have pain?
   A. Blood is building up in his lungs secondary to his decreased lung function.
   B. The lack of O_2 leads to inflammation, pain, and eventually cell death.
   C. He has a bad case of gastroesophageal reflux disease.

Answer: B. This patient is clearly having a left wall myocardial infarction. The lack of O_2 delivery to the cardiac muscle leads to ischemia and subsequent inflammation of the O_2-deprived cells. With inflammation comes pain. If the area of infarction is large enough and decreases the ability of the heart to pump out blood, some fluid could be potentially building up in his lungs. This however would not present as pain, but rather as dyspnea (i.e., difficult or uncomfortable breathing). Although gastroesophageal reflux can also cause chest pain, this patient's presentation is more likely to be secondary to a myocardial infarction.