Design of Respiratory Devices

in

Biomedical Engineers' Handbook

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Contents

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Introduction

Respiratory medical devices generally fall into categories designed to measure volume, flow, pressure, or gas concentration. Many of these devices have been used in some form for many years, so design is both sophisticated and incremental. A thorough knowledge of pulmonary physiology and existing devices can be very helpful when proposing improvements. Most respiratory devices are composed of one or more simpler components, often linked to a processing unit of some type, such as a stand-alone personal computer (PC). Remarkably varied and sophisticated diagnostic instruments can be constructed from these basic building blocks combined with values, tubing, pumps, and mouthpieces.

Pulmonary Physiology

Before delving too deeply into the instrumentation, it will be helpful to review briefly the function of the respiratory system and the parameters most often measured in pulmonary medicine.

The human respiratory system is composed of two lungs contained within the thorax, or chest-cavity. The primary function of the lungs is gas exchange with the blood, providing a continuous source of oxygen for transport to body tissues, and eliminating carbon dioxide produced as a

waste product of cellular metabolism. Gas exchange occurs in the alveoli, tiny thin-walled air-filled sacs numbering approximately 300 million in normal adult lungs. The alveoli are connected to the outside environment through a system of conducting airways that ends with the oral and nasal cavities. Alveoli are surrounded by and in close proximity to pulmonary capillaries, the tiny vessels containing blood to participate in gas exchange. The network of alveoli and airways is interdependent, so that the walls of the alveoli are shared among neighboring lung units.

Inspiration of fresh air occurs when respiratory muscles, chiefly the diaphragm, contract, expanding the chest wall and decreasing slightly the pressure surrounding the lungs but within the chest cavity (the *pleural pressure*). This drop in pleural pressure tends to pull outward on the outer lung surfaces, which in turn pull outward on more central lung units due to interdependence, and so on, with the result that the pressure within the alveolar air spaces falls. When alveolar pressure falls below the surrounding atmospheric pressure, air flows down the pressure gradient, filling the alveoli with inspired gas. Because lung tissue is elastic, it will tend to deflate when inspiratory muscle forces are released. In a normal person at rest, expiration is a passive phase and requires no muscular activity.

If all of a person's muscles were paralyzed and the lung was then permitted to empty, the lung volume would decrease to the *functional residual capacity* (FRC). At this volume, lung elasticity tends to favor further emptying, but the chest wall favors expansion. At higher volumes, both structures favor emptying [see Fig. 1]. FRC, then, represents an equilibrium between the tendency of the lungs to empty further and the tendency of the chest wall to spring

outward. In order to decrease the volume of the lung below FRC, expiratory muscles must be used to contract the chest wall and increase the pleural pressure. When the lung is emptied as much as is possible, there remains trapped within the alveoli and airways a volume of gas termed the *residual volume* (RV). The gas becomes trapped when the airways through which gas must travel collapse due to the high pleural pressure surrounding them. The amount of additional gas that may be expired with effort after the lung has reached FRC is termed the *expiratory reserve volume* (ERV). Thus, FRC is the sum of RV and ERV (FRC=RV+ERV).

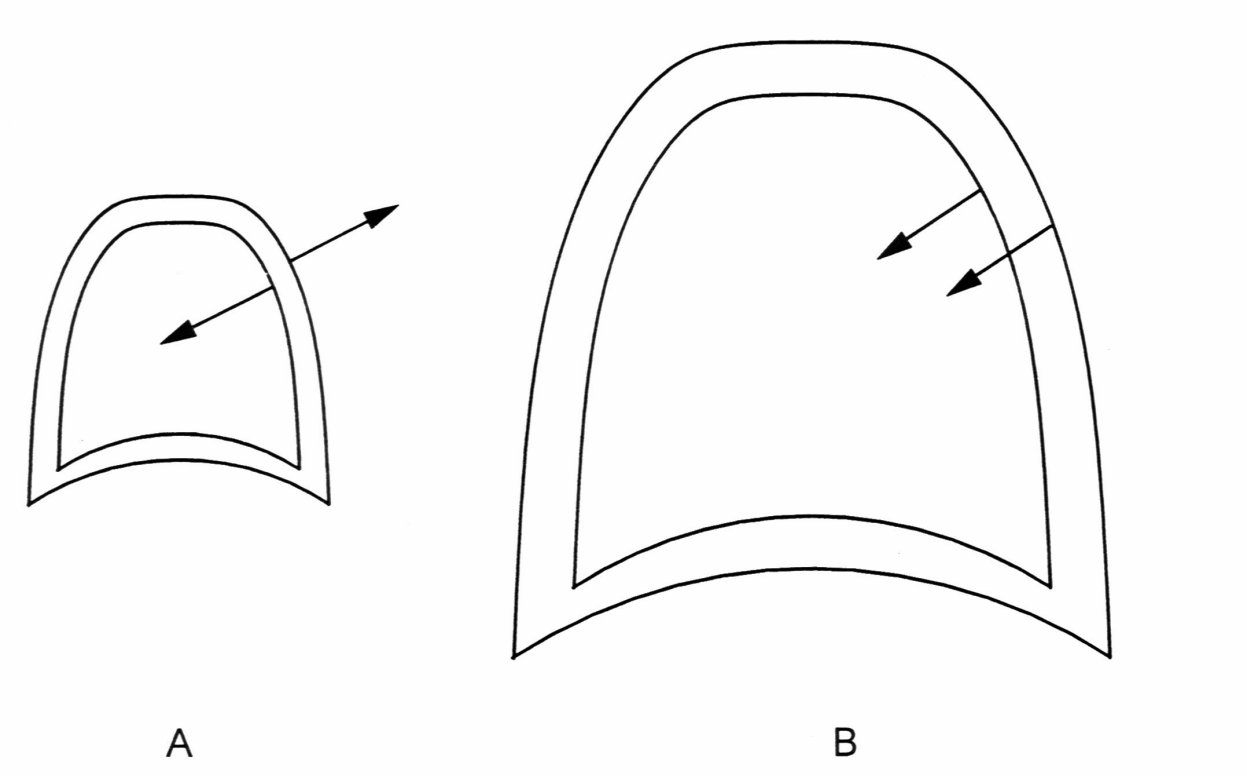

Figure 1. At lower volumes (A), the lung favors emptying, but the chest wall favors expansion. At higher volumes (B), both the lung and the chest wall favor emptying. The resting volume of the lung is below the residual volume; the resting volume of the chest wall is typically about 60% of TLC (see text).

During quiet breathing, passive expiration ends at FRC as the lung and chest wall reach equilibrium. The subsequent inspiration will increase the lung volume by an amount termed the *tidal volume* (TV), which is typically about 500 ml for an adult at rest. Of course, the normal

resting breath is far smaller than a deep breath; a maximum inspiration occurs when the lung is inflated to the *total lung capacity* (TLC), the largest volume that can be contained within the lung. TLC is determined by the balance between the increasing recoil (or "pull") of the lung and chest wall as they are inflated and the decreasing strength of the muscles as they are stretched. The difference between the TLC and the RV is termed the *vital capacity* (VC) and represents the largest volume of gas that can be exhaled, starting from full inflation, in a single breath. Thus, TLC=RV+VC. Figure 2 shows a diagram of the various lung volumes and capacities.

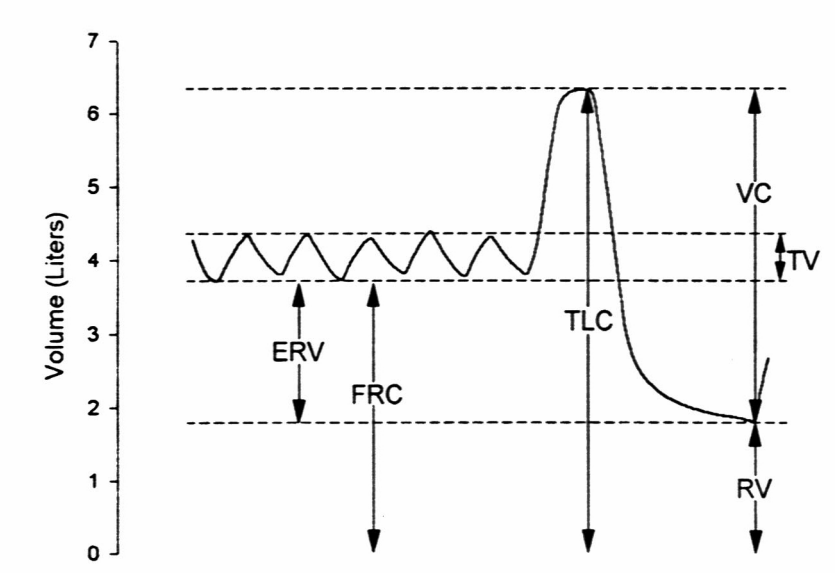

Figure 2. Spirometer tracing showing the lung volumes. Note that since the zero point of the spirometer may be set arbitrarily, only volumes not depending on zero (VC, TV, and ERV on this figure) may be measured directly.

Unlike TV, which is determined in large part by effort and ventilatory drive, TLC, RV, and VC are parameters that reflect certain properties of the pulmonary physiology. For example, a condition tending to increase the propensity of the airways to collapse would tend to increase the RV, and thereby decrease the VC, without changing the TLC. Asthmatics, in fact, may exhibit just this propensity during an asthma attack. Likewise, a condition increasing the elasticity (or "stiffness") of the lung would tend to decrease the TLC, and perhaps the VC, as the muscles

became unable to supply sufficient force for continued inspiration. One condition causing such a change is asbestosis. Measurement of the various static lung volumes can be helpful both in classifying a lung disease and in tracking its progress or responsiveness to treatment.

During the process of ventilation, gases must travel through the airways linking the alveoli with the nose and mouth. These airways impose a pneumatic resistance to the flow of air, which, similar to an electrical resistance limiting current, reduces the flow for a given pressure gradient. During quiet breathing, most of the resistance to airflow occurs in the upper airway and not in the smaller airways within the lung. The resistance of the airways themselves is affected by the volume of the lung at the time of measurement, because as the lung approaches full inflation, the airways are stretched radially, achieving their greatest diameter and hence their lowest resistance. Another lung parameter affecting both static and dynamic changes is the lung compliance, a measure of tissue elasticity. The compliance is defined as the change in volume divided by the change in pressure across the wall of the lung, has units of volume over pressure, and is typically measured as the slope of a plot of lung volume against transmural pressure. Even in a person having normal muscle strength, it is possible to have marked reductions in the static lung volumes (such as TLC, VC, and RV) because of increases in the stiffness of the lung tissue. Like the resistance, compliance depends on the volume of gas contained within the lung. As the lung volume approaches TLC, it takes considerably greater pressure to continue inflation when compared with similar inflations taken nearer to FRC, representing a reduction in lung compliance at higher lung volumes.

Similar to electrical resistance and capacitance, airway resistance and lung compliance together impose a frequency-dependent impedance to ventilation. Thus, the normal lung emptying passively follows an exponential decay with a single time constant equal to the product of the resistance and the compliance. Because the lung is composed of millions of lung units, potentially having regional differences in impedance, dynamic characteristics of ventilation affect how quickly the lung may inflate or deflate, and may also result in portions of the lung being under-ventilated, while other portions are either normally ventilated or even over-ventilated.

In addition to ventilating the alveoli, another important function of the respiratory system is gas exchange, the process of moving oxygen into and carbon dioxide from the blood supply. Gas exchange occurs through the passive diffusion of gases across the alveolar membrane. Diffusive gas exchange is affected by the thickness and permeability of the alveolar membrane, the total surface area available for diffusion, and the availability of blood flow to receive or deliver the diffused gases. One common pulmonary test, the *diffusion capacity*, indirectly assesses the alveolar membrane by measuring the diffusion of carbon monoxide from the lungs into the blood. Of course, gas exchange can occur only with gas that has actually reached the alveoli, which is considerably less than the amount of gas moving through the nose and mouth. In fact, in a normal person at rest, only about 2/3 of the air inspired in a single breath reaches the alveoli. The remaining 1/3 occupies the *dead space*, portions of the lung, airways, and nasopharynx that do not participate in gas exchange. In certain conditions, alveoli that are ventilated may not participate in gas exchange due to aberrations in diffusion or to alterations in blood flow that reduce or eliminate perfusion. These non-exchanging alveoli increase the *physiologic dead*

space (as distinguished from *anatomic dead space*, which comprises the mouth, nasopharynx, trachea, and other conducting airways) and reduce the alveolar ventilation. Dead space ventilation, then, is "wasted" ventilation and must be subtracted from the total ventilation in order to determine the effective alveolar ventilation.

Once the pulmonary circulation has undergone gas exchange with ventilated alveoli, the oxygen-enriched blood circulates to body tissues, which consume the oxygen and replace it with carbon dioxide. The net consumption of oxygen ($\dot{V}_{O2}$) is not equal to the net respiratory production of carbon dioxide ($\dot{V}_{CO2}$), owing to the fact that cellular metabolic pathways do not maintain a 1:1 balance between the two, and also to the fact that carbon dioxide may be excreted in the urine as well as through the respiratory system. At rest, the ratio of $\dot{V}_{CO2}$ to $\dot{V}_{O2}$, the *respiratory quotient* (RQ), is typically 0.7. During maximum exercise, this value may rise to well above 1.0. Measurements of $\dot{V}_{O2}$, $\dot{V}_{CO2}$, and RQ are important in assessing the adequacy of nutrition of a critically ill patient, the diagnosis and treatment of patients with various pulmonary and cardiovascular diseases, and the training of elite athletes.

Important Principles of Gas Physics

Most measurements made in the context of the respiratory system assume that the gas or gas mixture involved obeys the *Ideal Gas Law*:

$$P * V = n * R * T \quad (1)$$

where P =pressure (atmospheres, atm)

V =volume (liters, L)

n =moles of gas

T =temperature (Kelvin)

R =Gas Constant (= 0.082057 [atm•L]/[moles•Kelvin])

The amount of each gas present in a mixture of gases may be represented conveniently in several ways: by its percentage (or fraction) of the whole, by its absolute volume in a known total volume, or by its partial pressure. The partial pressure of a gas in a mixture is the pressure that would be exerted by that gas on the walls of its container in the absence of all other gases. According to *Dalton's Law*, the sum of the partial pressures of all gases present in a mixture is equal to the total pressure exerted by the mixture. For a gas mixture at atmospheric pressure, then,

$$P_B = \sum_{i=1}^{N} P_i \qquad (2)$$

where P_B =the ambient atmospheric pressure (typically ~760 mmHg at sea level)

P_i =the partial pressure of the i-th species

N =the total number of gases present in the mixture

The fractional concentration of a species is simply its partial pressure divided by the total pressure. Typical components of inspired and expired air are shown in Table 1.

Table 1

Constituents of Air

	Ambient		Inspired		Alveolar		Expired	
	mmHg	%	mmHg	%	mmHg	%	mmHg	%
Nitrogen (N_2)	584.1	76.86	556.8	73.26	566.2	74.50	583.7	76.80
Oxygen (O_2)	156.6	20.60	149.2	19.64	100.0	13.16	103.1	13.56
Carbon Dioxide (CO_2)	0.2	0.03	0.2	0.03	40.0	5.26	41.2	5.43
Water (H_2O)	12.0	1.58	47.0	6.18	47.0	6.18	25.0	3.29
Other	7.1	0.93	6.8	0.89	6.8	0.89	7.0	0.92

Assume ambient temperature of 24°C, ambient relative humidity of 50%, barometric pressure of 760 mmHg, and body temperature of 37°C.

Special note must be made of the presence of water vapor as it presents an often-overlooked factor. The amount of water a gas mixture is *capable* of containing is limited by the availability of water and the temperature of the mixture. The relative humidity measures the percentage of this upper limit actually achieved. The relationship between temperature and the maximum possible partial pressure of water has been determined empirically; one suitable equation over common temperature ranges is

$$P_{H2O} = 14.47 - 0.705 * T + 0.0428 * T^2 \quad (3)$$

where P_{H2O} =partial pressure of water vapor (mmHg)

T =temperature (Celsius)

At room temperature, the maximum possible P_{H2O} is approximately 25 mmHg. The maximum possible P_{H2O} rises to about 47 mmHg as the temperature rises to normal body temperature (37 C). Thus, upon inspiration, a sample of air is warmed and humidified, while expiration leads to cooling and condensation of excess water vapor. This is important for several reasons. First, the concentration of a gas as it exists within the lung differs from that in the air prior to inspiration or following expiration, as it is diluted or concentrated by changes in water vapor concentration.

Second, even if a known fixed volume of gas is injected into the lung, such as by a ventilator, the volume of the lung does not increase by that same volume. Lastly, a warm moist gas which is exhaled undergoes cooling and condensation, and even if re-warmed will not reach 100% relative humidity and will therefore contain less water than initially, unless a source of water is available as the gas is re-warmed.

The combined effects of changes in temperature, pressure, and water vapor concentration are frequently accounted for by applying an appropriate correction factor, calculated as shown in Table 2.

Table 2

Gas Conversion Factors (Volume and Flow)

To Convert From	To	Multiply By	
		Formula	Typical Value
ATPS	BTPS	$\frac{BP - pH_2O}{BP - 47} * \frac{310}{273 + T}$	1.080
	STPD	$\frac{BP - pH_2O}{760} * \frac{273}{273 + T}$	0.892
	ATPD	$\frac{BP - pH_2O}{BP}$	0.971
ATPD	BTPS	$\frac{BP}{BP - 47} * \frac{310}{273 + T}$	1.113
	STPD	$\frac{BP}{760} * \frac{273}{273 + T}$	0.919
	ATPS	$\frac{BP}{BP - pH_2O}$	1.030
BTPS	STPD	$\frac{BP - 47}{760} * \frac{273}{310}$	0.826
	ATPS	$\frac{BP - 47}{BP - pH_2O} * \frac{273 + T}{310}$	0.926
	ATPD	$\frac{BP - 47}{BP} * \frac{273 + T}{310}$	0.899
STPD	BTPS	$\frac{760}{BP - 47} * \frac{310}{273}$	1.210
	ATPS	$\frac{760}{BP - pH_2O} * \frac{273 + T}{273}$	1.121
	ATPD	$\frac{760}{BP} * \frac{273 + T}{273}$	1.088

BP =Barometric Pressure
T =Temperature (°C)

ATPS =Ambient temperature and pressure, saturated
ATPD =Ambient temperature and pressure, dry
STPD =Standard temperature and pressure, dry
BTPS =Body temperature and pressure, saturated

The "typical values" assume a barometric pressure of 760 mmHg and a temperature of 24°C.
Standard pressure is 760 mmHg and standard temperature of 0°C (=273 K).
Body temperature is 37°C (=310 K).

Under ideal conditions, seldom encountered, gas flowing through a straight tube would exhibit only *laminar flow* (the absence of all turbulence). In laminar flow, every molecule in the gas stream has only axial velocity, and moves only in the direction of the bulk flow. Under

conditions of complete turbulence, the gas molecules move in all directions, with no net flow. Flows encountered in practice exhibit some characteristics of both laminarity and turbulence [Fig. 3]. Factors tending to favor increasing turbulence include decreasing tube radius, increased gas density, and increasing bulk flow rate. Turbulence is increased by sharp angles and geometric obstructions in the gas stream. Laminar flow is increased by having a straight, smooth-bore tube with a length at least six times its diameter prior to flow measurement.

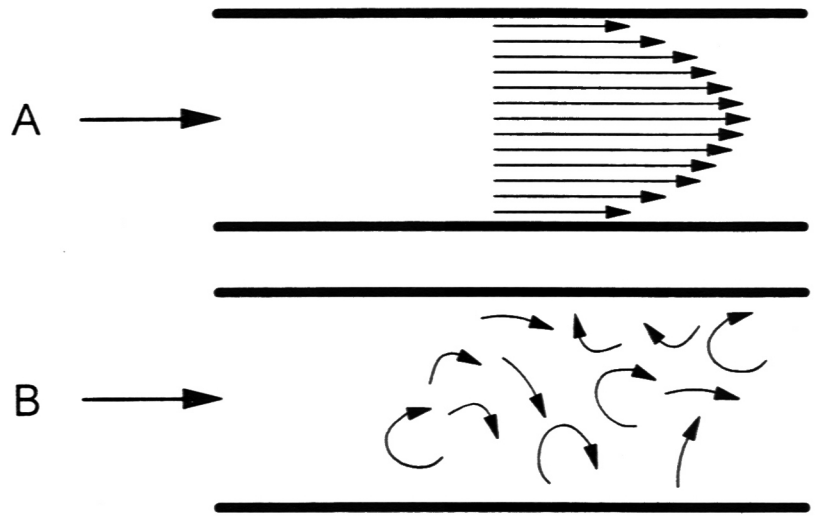

Figure 3. Representations of laminar (A) and turbulent (B) flow through a straight tube. With laminar flow, the pressure drop across a length of tube is proportional to the flow. With turbulence, the pressure approaches proportionality with the square of flow. The velocity profile under laminar flow conditions is parabolic, with higher flows near the center of the tube than near the boundary.

The pressure required to move gas along a straight tube under conditions of laminar flow is given by the Poiseuille equation:

$$\Delta P = \frac{\dot{V} * 8 * \eta * l}{\pi * r^4} \tag{4}$$

where ΔP =pressure drop

$\dot{V}$ =flow

η =gas viscosity

l =length of tube

r =radius of tube

Thus, for a given straight tube, Poiseuille's equation predicts a linear relationship between pressure and flow and gives rise to the pneumatic analog of Ohm's Law:

$$\Delta P = \dot{V} * R \qquad (\text{compare with } \Delta V = I * R) \tag{5}$$

where R =resistance, given by $8*\eta*l/\pi*r^4$

This Ohm's Law representation of the pressure-flow relationship forms the basis for measurements of airways resistance and is the principle on which several flow-measuring devices are based. The pressure required to move gas under conditions of turbulence is always greater than that required to achieve the same flow under laminar conditions, as additional pressure (or energy) is required to accelerate molecules in directions other than the direction of bulk flow. This will be manifested as an upward curve and deviation from linearity on a plot of flow (x-axis) versus pressure drop (y-axis).

Turbulence in flow through a straight tube may be estimated by calculating the *Reynold's Number:*

$$N_R = \frac{2 * s * r * \rho}{\eta} \tag{6}$$

where N_R =Reynold's Number

s =linear velocity of flow

ρ =gas density

and other variables are as shown above

Reynold's Numbers greater than 2000 are predictive of significant turbulence. It should be noted that while turbulent flow depends on both gas density and viscosity, laminar flow depends only on viscosity.

Device Components

Volume

Gas volumes may be measured directly using one of several volume displacement *spirometers*. The simplest and oldest design, the water-sealed spirometer, uses a hollow cylinder, or bell, which is inverted and lowered into a bucket of water containing a tube for the movement of gas [Fig. 4]. The bell rises or lowers as gas moves into or out of the gas space trapped between the bell and the water. In order to prevent excess compression of the gas within the bell, earlier models used a chain and counter-weight, although newer models are designed with lightweight bells in which gas compression is not significant. A pen is often attached to the bell, which may graph the volume-time tracing on an attached *kymograph*, a rotating drum with recording paper. Many spirometers also incorporate a linear potentiometer attached to the bell for easy electrical recording via a simple amplifier. The basic principle of operation is that the height of the bell is related to its volume by the formula for the volume of a cylinder:

$$V = \pi r^2 h \qquad (7)$$

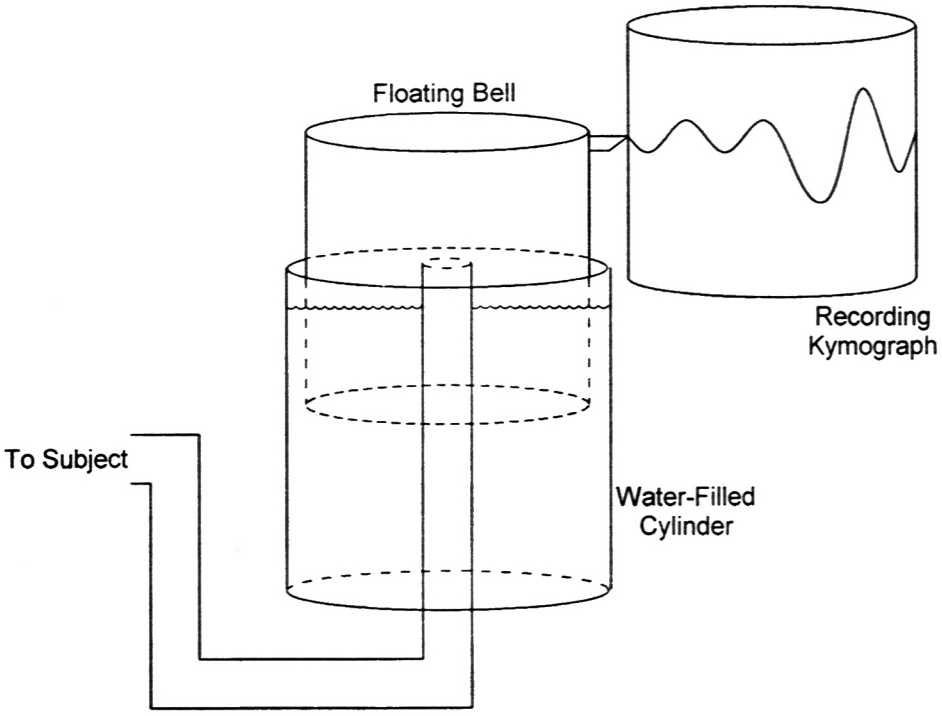

Figure 4. Schematic drawing of the water-sealed spirometer. The kymograph rotates at a constant speed, allowing for the inscription of a volume (y-axis) versus time (x-axis) plot as the bell moves up and down in response to gas movement at the outlet.

A similar approach is used in the dry-seal spirometer. In this case, the bell is sealed to its base with a thin layer of latex (or some other thin and flexible material). As gas is introduced into the bell, the latex prevents its escape and forces the bell to move, as with the water-sealed spirometer. Dry-seal spirometers may be mounted horizontally, and may employ a moving piston instead of a moving bell. Manual and electrical recording are achieved as with the water-sealed spirometer. A third type of volume displacement spirometer, less common in recent times, is the bellows, or wedge, spirometer. In this device, the gas to be measured is contained within a bellows whose expansion is recorded via a pen or a rotational potentiometer.

Volume displacement spirometers offer the advantage of simple construction and use. They do not require computers or processors for simple volume and time measurements. Perhaps most importantly, they are easy to calibrate and do not depend on the composition of gases they are used to measure. However, they do suffer from some disadvantages. First, they are bulky. Water-sealed spirometers, in particular, can be heavy when they are filled with water, and they are prone to spillage when tipped. Second, owing to their mechanical action, they have a limited frequency response and are not well suited to rapidly changing signals (although they do have satisfactory frequency response for most common measurements). Last, the maximum volume they can measure is limited by their size. Thus, for an experiment in which tidal volume is measured over a period of five minutes, the volume displacement spirometer would be difficult to employ, without a series of complicated valves, as it would be filled before the experiment was over. Nevertheless, the volume displacement spirometer remains popular for simple measurements of volume and time.

A completely different approach, applicable only to volumes of gas as inspired or expired from the body, relies on the changes in chest (and sometimes abdominal) geometry that accompanies breathing. One design uses two elastic bands, one placed around the chest, the other around the abdomen. The bands contain strain gages that measure the relative expansion of each of the compartments. This device requires calibration with each patient or subject on whom it is to be used. It is affected by movement artifact, changes in patient position, or changes in the relative movements of chest and abdomen during breathing. It is best employed on patients at rest, during quiet breathing, such as during sleep. Its accuracy seldom exceeds +/- 20%. A similar device uses electrodes placed on the chest wall to measure trans-thoracic impedance as a means

to estimate changes in chest geometry. These devices offer the advantage of easy long-term measurements without the need for mouthpieces or other cumbersome connections, but their relative inaccuracy limits their usefulness.

Flow

Flow is the time-derivative of volume, or

$$\dot{V} = \frac{dV}{dt} \tag{8}$$

Thus, any device capable of measuring either volume or flow can also report the other, given an appropriate time measurement and the needed processing. For this reason, and others given below, flow measuring devices have become popular methods for measuring both volumes and flows (but, volume displacement spirometers also can easily calculate and report flow measurements).

There are three common groups of flow measuring sensors. The pressure-drop pneumotachometers rely on the Poiseuille equation by imposing a fixed resistance on the gas flow and measuring the pressure drop across the resistance. Assuming laminar flow, the pressure drop will be linearly related to the flow rate. The resistive element may come in several forms, but two of the most common are the Lilly and the Fleisch [Fig. 5]. The Lilly type uses a fine screen (similar to a window screen) to provide resistance. Often, three screens are used, with the outer screens meant to maintain laminar flow and to prevent debris and exhaled droplets from

damaging the middle screen. The Fleisch type uses a group of small parallel tubes as its resistive element.

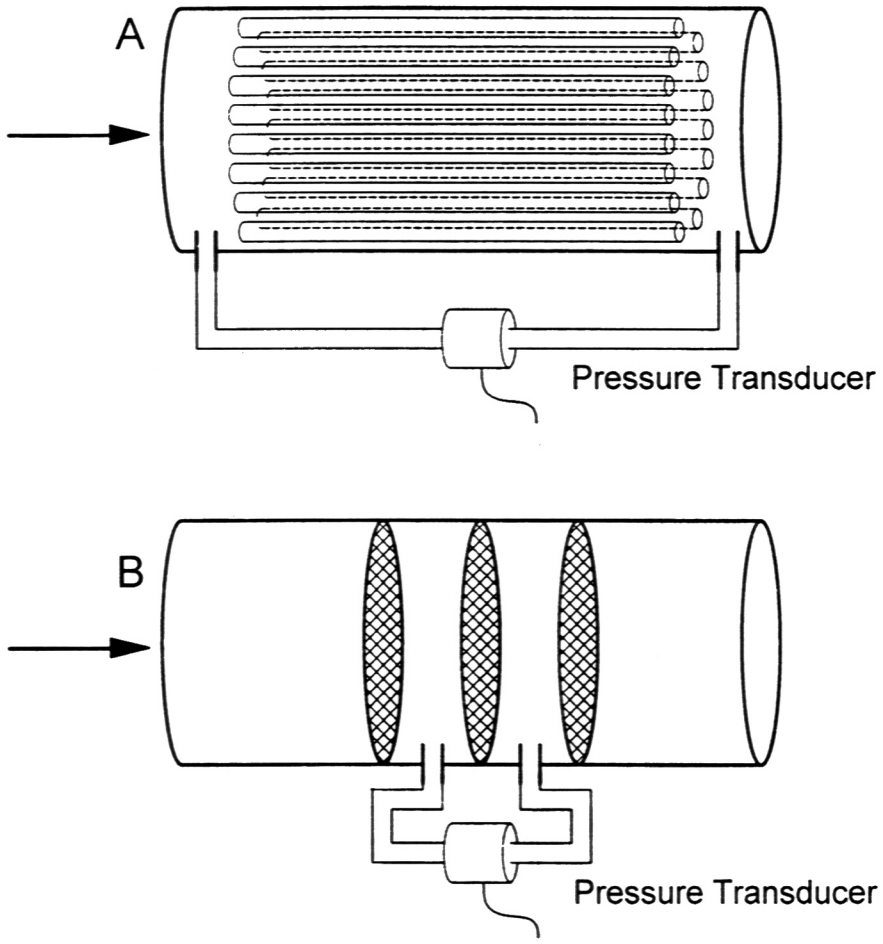

Figure 5. Schematic representations of the Fleisch (A) and Lilly (B) types of pneumotachographs for measuring flow. In both types, the small open ports are connected to opposite sides of a differential pressure transducer. The pressure difference between the open ports is related to the flow through the device by an equation that depends in part on the degree of turbulence present (see text).

In their simplest designs, both types rely on laminar flow to maintain a linear output. Thus, they may be rated for a maximum flow rate, above which linearity is compromised, as predicted by increases in the Reynold's Number. In practice, deviations from linearity are often seen even below the maximum rated flow. Sometimes this may be due to sub-optimal geometry between

the device and the connecting tubes and valves. Another cause of inaccuracy may be condensation of water from the warm moist exhaled gas as it contacts the colder surfaces of the pneumtachometer. In addition to causing computational difficulties because of changes in gas volume as water vapor is lost, the condensed water that is deposited on the resistive element may change its resistance and diminish its accuracy. This is often countered by heating the device to body temperature, thus preventing condensation. The reliance on linearity minimized the usefulness of this class of device until sufficient portable processing power was available that linearity no longer was required. Most devices now used no longer assume linearity, but instead characterize the flow versus pressure relationship over the entire useful range. This may be done by measuring the response to a series of known flows, but is more often calculated using an algorithm described by Yeh and colleagues [1981] using a calibration syringe of known volume. Under conditions of laminar flow, where only gas viscosity is important, the specific composition of the gas being measured is of little concern, since most gases present in common respiratory measurements are of similar viscosity [see Table 3]. However, if gases with a different viscosity will be used, the device must be carefully calibrated with gases having that same composition.

Table 3

Physical Constants of Common Respiratory Gases

	Viscosity	Density	Thermal Conductivity	Magnetic Susceptibility
	Micropoise	g/Liter	[Cal/(sec)(cm^2)(°C/cm)] x 10^{-6}	cgs units x 10^{-6}
N_2	178.1	0.625	56.20	-12.0
O_2	201.8	0.714	57.24	3449.0
CO_2	148.0	0.982	33.68	-21.0
He	194.1	0.089	333.50	-1.88
H_2	87.6	0.089	405.00	-3.98
CO	175.3	0.625	53.85	-9.8
Ne	311.1	0.446	107.03	-6.74
CH_4	108.7	0.446	71.08	.

All values taken near room temperature (19°C - 30°C) from tables in CRC Handbook of Chemistry and Physics, Robert C. Weast, ed., 61st edition, 1981.

A different variety of pressure drop flow sensor relies on the Pitot effect instead of Ohm's Law. In one design of this type of device, two pressure sensing "taps" are placed within the gas stream, one pointed directly upstream and the other pointed directly downstream [Fig. 6]. The pressure difference is no longer described by the Poiseuille equation, but rather is described by Bernoulli's Law, which states that the pressure difference between the taps is a function of the density of the gas measured and the square of its velocity. Velocity is related to volumetric flow by the cross-sectional area of the apparatus. Because this device is affected by gas density, it is usually employed in conjunction with analyzers providing precise measurements of the types and concentrations of gases present, allowing for calculation of the mixture's density, but limiting the device's usefulness as a stand alone flow sensor.

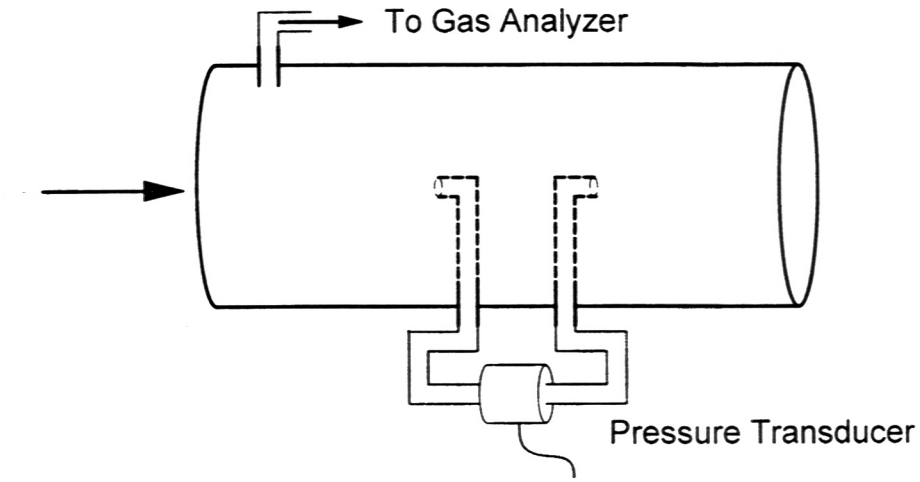

Figure 6. Schematic representation of a Pitot tube. Some designs incorporate elements to better control the degree of turbulence. The gas analyzer is used to measure the density of the gas (see text).

The second group of flow measuring sensors, commonly referred to as hot wire anemometers, is based on the principle that flowing gas will cool a heat source, and that greater flows will cause greater cooling of the heat source. The devices contain a heated wire (some designs incorporate a second heated wire, at a different temperature, as a reference), which is maintained at a constant temperature via feedback circuitry [Fig. 7]. The current required to maintain the stable temperature is related to the bulk flow through the device. The hot wire anemometer is affected slightly by the thermal conductivity of the gases present, but is less sensitive to changes in gas composition than pressure drop flow sensors. The accuracy of this type of flow sensor, too, is affected by increasing turbulence.

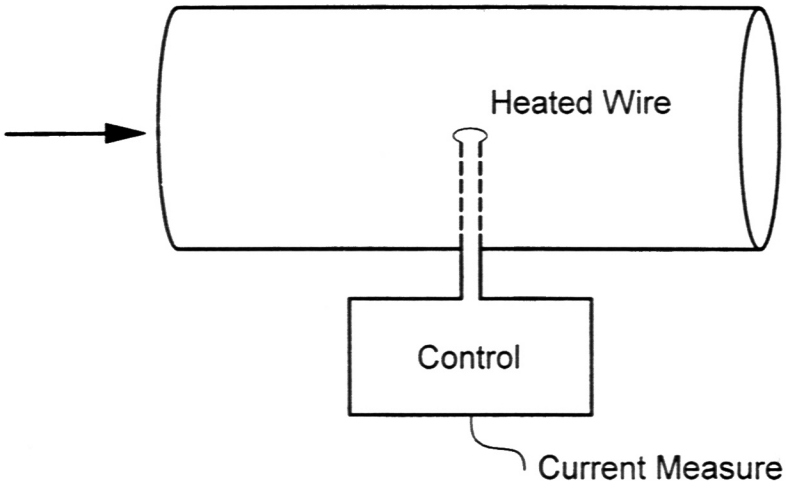

Figure 7. Schematic representation of a hot-wire anemometer. The flow is related to the current required by the feedback control circuitry to maintain the heated wire at a constant temperature.

The third group of flow sensors are the turbines, devices that are based on a rotating vane placed in the gas stream, much like a wind speed indicator on a simple weather station. The rotation of the vane is proportional to the velocity and density of the gas stream. As with the Pitot effect devices, gas velocity is related to volumetric flow by the cross-sectional area of the apparatus. Turbine flow sensors can be purely mechanical, with precision gearings and a display dial, making for a very portable device requiring no electricity. Battery-powered models using an LED and a light sensor to count the rotations of the vane are also common. Turbine sensors must overcome several challenges to remain accurate, however. First, the moving parts must be lightweight to reduce the effects of inertia, which tend to impair the frequency response of the device. At the same time, however, the vanes must be made strong enough to withstand the forces of high flow rates.

The chief advantages of flow sensors are their small size and their ability to measure continuously in flow-through designs. They all offer good dynamic range, with frequency responses that exceed that needed for most or all respiratory measurements. They suffer from the need for more complex calibrations and generally require a computer or processor unit. The Pitot effect device requires simultaneous measurement of gas concentrations. The hot wire anemometer requires external circuitry capable of heating the wires sufficiently and somewhat sophisticated feedback circuitry. The turbine sensors can be fragile and susceptible to damage.

Pressure

Although there are a variety of pressure transducer types available, for most respiratory applications the newer solid-state pressure transducers offer the most attractive alternative. Variable capacitance transducers generally use the deflection of conductive plates by the input pressure differential to generate an output signal. Similarly, variable inductance transducers use the input pressure differential to create a change in inductance. In both cases, the transducer requires an input AC excitation signal in order to create an output signal. The circuitry used to create the excitation, and to output a usable pressure signal, is often referred to as a carrier-demodulator. These types of transducers are very precise, offer a large variety of input ranges, and maintain stable calibrations. However, they can be somewhat expensive and require dedicated external circuitry.

Solid state pressure transducers come in a single package, often quite small, and also offer a wide choice of input pressure ranges. Typically, they use the input pressure differential to deform slightly a semi-conductor plate separating two chambers exposed to each of the two input pressure levels. Any difference between the two levels will deform the separating plate, changing its conductive properties. On board circuitry usually allows the transducer to accept a DC excitation voltage, and provides a linear, temperature-corrected DC output voltage. These transducers are offered by a large number of vendors at affordable pricing.

All of these pressure transducers offer frequency response characteristics acceptable for most or all respiratory applications. In situations requiring the measurement of a single pressure (for example, the pressure at the mouth during breathing), one of the two input ports to the transducer is left open to atmospheric pressure. In other situations requiring the measurement of a pressure differential (for example, measuring the output of a pressure-drop flow sensor), the two ports of the transducer are attached to the two taps of the sensor.

Gas Concentration

There are a large number of gas analysis technologies available to measure the concentrations of various species present in a gas mixture. Some of the more common types used in respiratory applications are based on principles of *thermal conductivity*, *infrared absorption*, *zirconium fuel cell technology*, *paramagnetism*, *emission spectroscopy*, *gas chromatography*, and *mass spectrometry*. In many cases, some gases in a mixture interfere with the analysis for other gases and must be removed. Most often, interfering gases to be removed are water vapor and carbon

dioxide. Water vapor may be removed by passing the gas stream through a canister of calcium sulfate [$CaSO_4$]. Alternatively, water vapor may be removed, or equilibrated to a known level, by passing the gas mixture through a length of nafion, tubing with walls that are able to remove water because they are impregnated with a material with a high affinity for water. Placing the nafion within the lumen of larger tubing through which is run dry nitrogen (running in the direction opposite to the gas mixture to be analyzed) will remove all the water vapor from the mixture, whereas leaving the nafion tubing exposed to room air will equilibrate the water vapor concentration with ambient levels. Carbon dioxide is most often removed by passing the gas stream through a canister containing either barium hydroxide [$Ba(OH)_2$] or sodium hydroxide [NaOH]. In both cases, the chemical combines with the gaseous CO_2 removing it from the gas mixture. Also, both chemical CO_2 scrubbers produce water as a by-product of the reaction and therefore should be placed upstream to a water removal system if needed. Usually, any chemical scrubber will be impregnated with an indicator that changes color as the chemical becomes consumed, alerting the user to the need for replacement.

Thermal conductivity meters measure the ability of a gas mixture to conduct heat away from a heat source [Fig. 8]. They usually employ two thermistors, one exposed to sample gas and the other to a reference sample containing none of the gas to be measured, arranged in a conventional Wheatstone bridge. Thermal conductivity is most commonly used to measure helium concentration, although it can be used to measure carbon dioxide concentrations if used carefully. Both carbon dioxide and water vapor interfere with helium analysis and must be removed from the gas mixture prior to helium analysis. Water vapor, like helium, has a higher thermal conductivity than other gases found in air and thus will cause false elevation in the

helium reading. Carbon dioxide, on the other hand, has a lower thermal conductivity and will cause a lowered helium reading. Thermal conductivity meters tend to be quite linear, making them easy to use, but they have relatively slow response times on the order of 20-30 seconds.

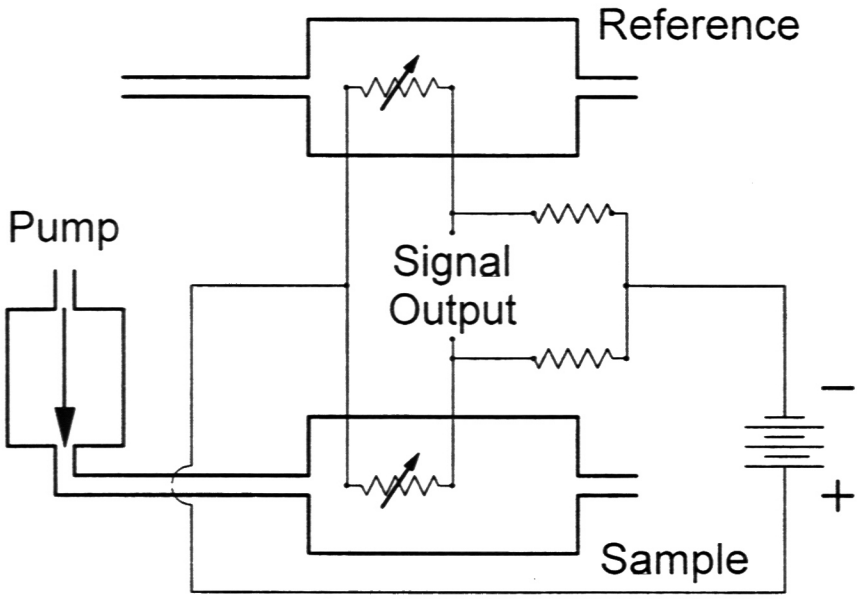

Figure 8. Schematic drawing of a thermal conductivity meter. The electrical elements are configured in a typical Wheatstone bridge circuit. The variable resistors are usually thermistors.

Infrared (IR) absorption is a common method of gas analysis and can be used for measurements of carbon dioxide, carbon monoxide, and methane [Fig. 9]. IR analyzers run the gas mixture through a sample chamber illuminated at one end with an IR light source. At the other end of the chamber is an IR detector. Parallel to the sample chamber is a reference chamber, which is usually filled with room air and uses the same IR source and detector as the sample chamber. The gases to be analyzed absorb some of the IR radiation, decreasing the amount reaching the detector. A motor rotates a "chopper blade" which alternately blocks one of the two chambers

from the source. By synchronizing the chopper rotation with the signal at the detector, the analyzer can determine the relative absorption in the reference chamber. This synchronization can be achieved by using a standard LED and light detector to determine the position of the chopper opening. The IR analyzer is sensitive to the pressure within the sample chamber, and thus requires either a constant flow through the chamber using a stable pump, or no gas flow after a pump has filled the chamber with the gas to be analyzed. IR analyzers can be designed to have rapid response times. When used as a CO analyzer, CO_2 is an interfering gas and must be removed or subtracted mathematically. H_2O is an interfering gas for almost all other gases and should be removed or equilibrated prior to analysis.

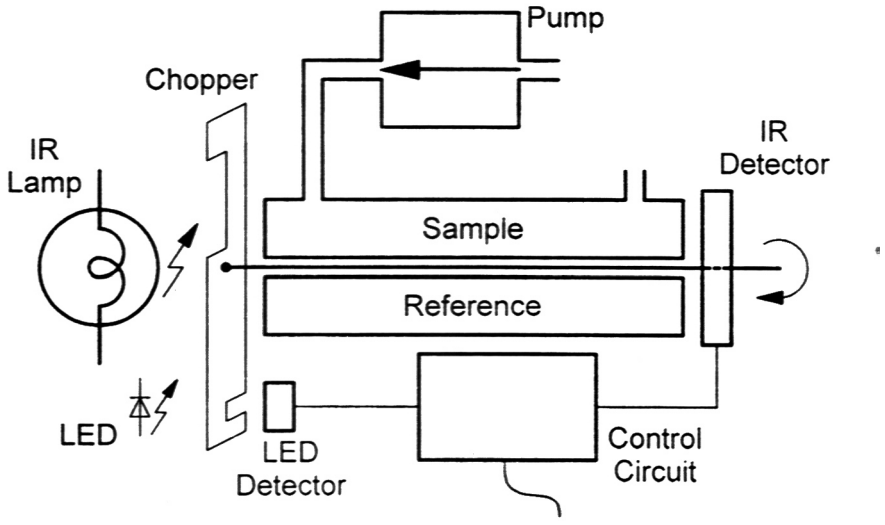

Figure 9. Schematic showing the function of an infrared (IR) gas analyzer. The "chopper" rotates, allowing light from the IR lamp to illuminate only one of the two gas-filled chambers (sample and reference) at a time. The IR light passes through the illuminated chamber, where it is differentially absorbed by the gases present. The IR detector measures the amount of IR light transmitted through the whole chamber. The LED and LED detector allow the control circuit to determine which of the gas-filled chambers is illuminated at any time. The control circuit measures and linearizes the differential IR absorbance of the two chambers, and outputs the usable signal.

The zirconium fuel cell employs a zirconium substrate coated by platinum to create an electrode sensitive only to oxygen [Fig. 10]. Oxygen diffuses through the platinum coating on one side,

passes through the zirconium, and completes the circuit on the other side of the fuel cell. So long as there is an oxygen concentration difference on the two sides, the movement of oxygen ions creates a current and induces a voltage, which is logarithmically related to the oxygen concentration difference. The zirconium is heated to high temperature (> 700 C), requiring adequate warm up time (20-30 minutes) and power requirements not suited to highly portable applications. The analyzer is sensitive to the pressures within it and thus requires a stable sample flow. It offers a rapid response time and is relatively insensitive to interfering gases.

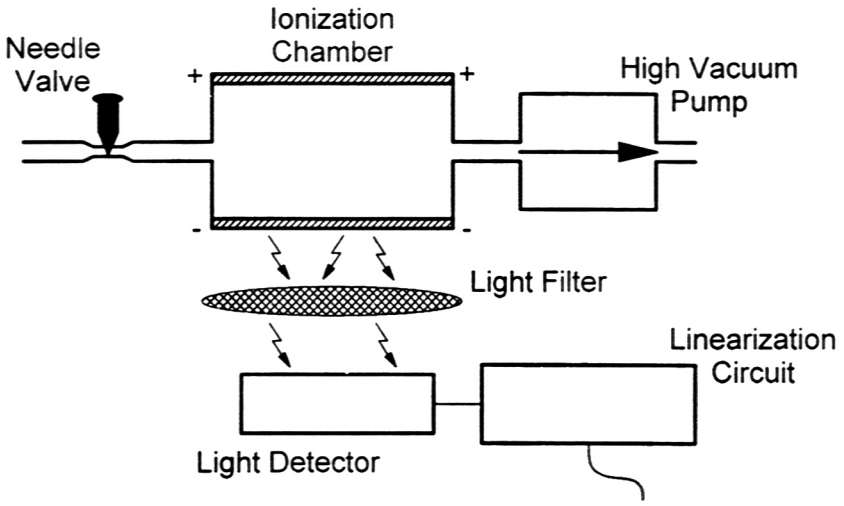

Figure 10. Schematic drawing of an emission spectroscopy analyzer, typically used to measure nitrogen concentrations. The output varies with the pressure within the ionization chamber, so the needle valve and vacuum pump must carefully regulate that pressure.

Paramagnetism refers to the propensity for certain molecules to align themselves when exposed to a magnetic field. Oxygen exhibits very high magnetic susceptibility compared to other common respiratory gases. The paramagenetic oxygen analyzer introduces a gas mixture into a hollow dumbbell-shaped structure suspended in a magnetic field. The greater the oxygen content, the greater the force tending to move the dumbbell toward alignment in the field. The oxygen concentration may be measured either as the deflection of the dumbbell or as the force

required to prevent the dumbbell from moving. The analyzer is sensitive to pressure, and thus flow rates must be held steady during measurement. Response times on modern analyzers are quite fast and may be suitable for rapid sampling.

Emission spectroscopy is used to measure nitrogen concentrations. Nitrogen is drawn via a strong vacuum through a needle valve into a *Giesler tube*, a very low pressure chamber where it is exposed to a strong electric field (on the order of 25 kV). The N_2 ionizes and emits light, which is filtered and picked up by a photodetector, where the signal is amplified and linearized, and output to a recorder. The output is quite sensitive to the pressure within the chamber and thus the vacuum pump and needle valve must both be quite stable. This type of nitrogen analyzer has a rapid response time and is relatively insensitive to interfering gases. However, achieving and maintaining the required vacuum can be challenging to the designer. An alternative approach to the analysis of nitrogen concentration is to measure O_2 and CO_2 concentrations and, if water vapor pressure has been removed, calculate the remainder to be nitrogen (assuming no other gases are present).

Gas chromatography separates a mixture of gases by passing the sample through a column containing a material, which selectively impedes the progress of different species along its length [Fig. 11]. The gas sample is mixed with a "carrier" gas (usually helium, rendering this type of analyzer unable to measure helium concentrations) and run through the column. Species that are less impeded by the column material exit the column first, followed sequentially by other species. The concentrations of the now separated species are measured using another type of detector, frequently a thermal conductivity meter. Water vapor is usually removed prior to

passing the gas through the column. The gas chromatograph offers the advantage of being able to measure several different gases with one analyzer, but has relatively slow response times and is unsuitable for continuous sampling with changing inputs.

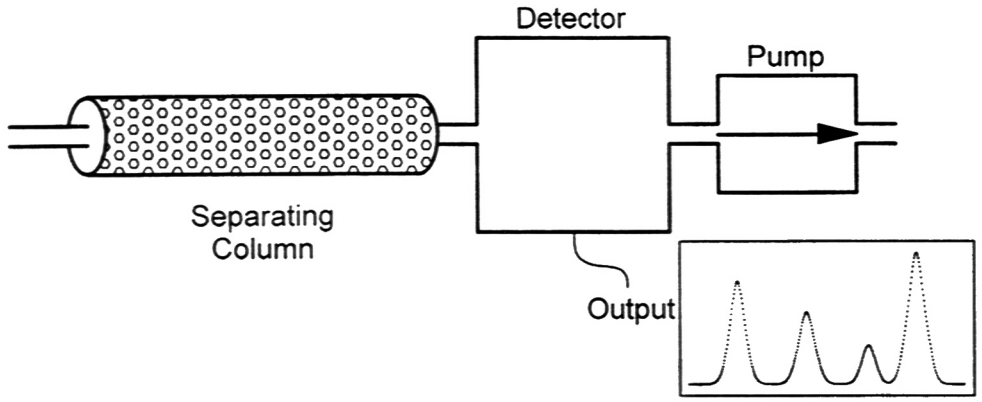

Figure 11. Schematic diagram of a gas chromatography (GC) analyzer. The gas mixture to be analyzed is drawn through the column where it is separated into its constituent species. The separated gases are then drawn through another gas detector (often a thermal conductivity analyzer) where concentrations are measured.

The mass spectrometer, like the gas chromatograph, is capable of measuring many or all constituents in a gas mixture within a single analyzer. The gas mixture is drawn via a vacuum into a low pressure chamber where its molecules are ionized by an electron gun [Fig. 12]. The charged ions are accelerated by an electric field down a chamber, and are then exposed to a magnetic field. The ions are deflected along an arc by the magnetic field according to their mass and charge: larger ions exhibit a greater radius of curvature than smaller ions with the same charge. Detectors count the number of ions at various locations within the analyzer. Because the analyzer distinguishes species based on molecular mass, different molecules with the same mass cannot be separated. The mass spectrometer has an extremely rapid response time and is well suited to continuous sampling and measurement. It is, however, quite large and expensive. Water vapor is usually removed from the gas stream prior to analysis.

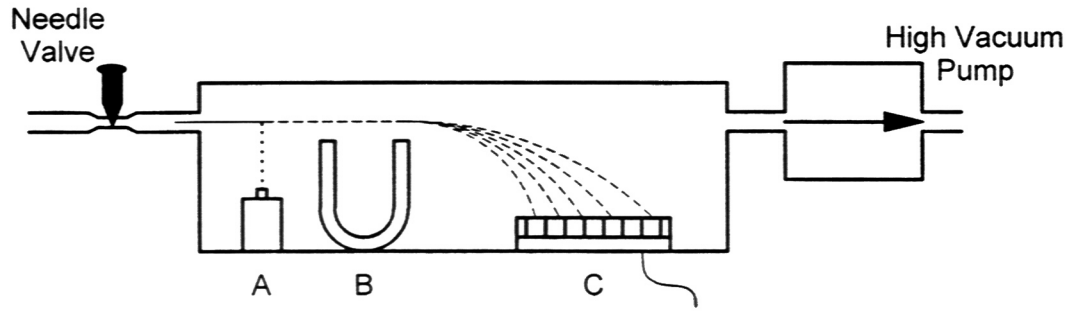

Figure 12. Schematic drawing of a mass spectrometer. The gas is ionized by an ion gun (A) and then passes through a magnetic field (B). The charged particles follow a circular path with a radius dependent on the mass-to-charge ratio. The collector (C) is composed of a series of particle detectors at various distances along it length. Each detector's output indicates the concentration of a different gas species. The spectrometer collector does not distinguish between ionized particles having the same mass-to-charge ratio, and thus there are certain gases which cannot be analyzed separately.

All of the gas analyzers described above have been used successfully in clinical practice. Although they all have advantages and disadvantages, all are suited to certain types of applications.

Common Respiratory Measurements

Putting the preceding discussions into practice is the everyday mission of the *Pulmonary Function Laboratory*, a common clinical unit designed to make respiratory measurements on hospital patients and research subjects. Some of the most common measurements and the devices used to make them will be described below.

Spirometry

Spirometry is the most common respiratory measurement and reports, in a single maneuver, a remarkable range of valuable parameters. In this test, the patient inspires fully to TLC and then expires rapidly and forcefully, blowing hard until the lung volume reaches RV. A tracing of volume versus time is obtained, from which many parameters may be measured, including FVC, FEV_1 (the volume of air exhaled during the first second), and the ratio of FEV_1/FVC [Fig. 13]. Spirometry also reports the maximum, or peak, expiratory flow, as well as instantaneous flows at specified lung volumes. Spirometry may be performed using a volume displacement spirometer, with electrical or mathematical differentiation to measure flows, or using a flow sensor with mathematical integration to obtain volumes. Standards for spirometry have been published by numerous medical societies. For such a simple to perform test, spirometry is remarkably powerful. It is exceedingly reproducible when compared with other medical tests. It is commonly used for a wide variety of medical purposes, including the detection and classification of various forms of lung disease, the responsiveness to various therapeutic interventions, and the progression of pulmonary and non-pulmonary conditions. Indeed, the FEV_1 has been shown in numerous studies to correlate more reliably with mortality than many other common medical tests, for reasons not completely understood. All spirometric parameters are reported at BTPS conditions.

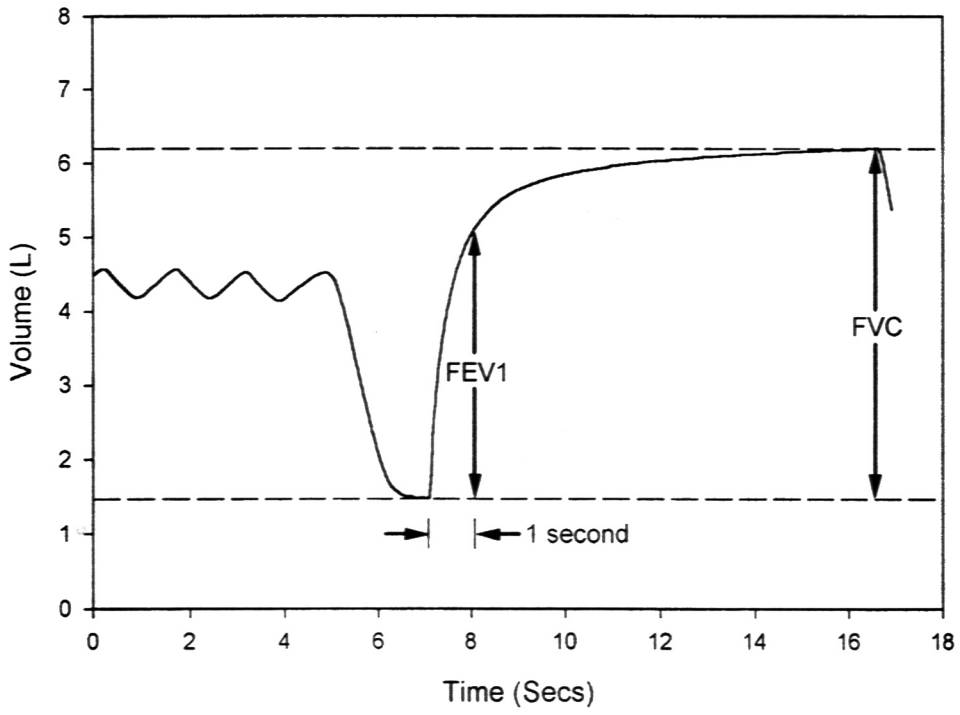

Figure 13. Spirometer volume-time tracing typical of spirometry during forced expiration. In this representative test, the FEV1 is 3.64 L and the FVC is 4.73 L.

CO Diffusing Capacity

The CO diffusing capacity, DLCO, is calculated by measuring the difference in alveolar CO concentrations at the beginning and end of a period of breath holding. The test begins by having the patient exhale completely to RV and then inspiring rapidly to TLC a breath of gas with a known CO concentration. After a ten-second breath-hold, the patient exhales rapidly [Fig. 14]. The initial portion of this exhalation is discarded, as it contains gas from the dead space, and a portion of the subsequently exhaled gas, assumed to be well-mixed alveolar gas, is analyzed for

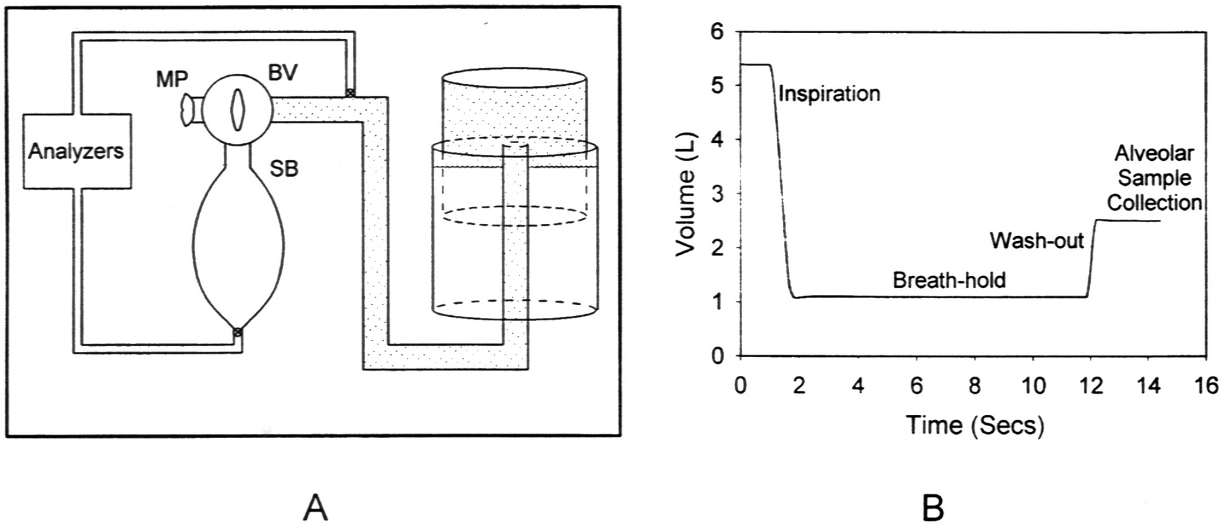

Figure 14. Illustration of equipment for performing a single-breath diffusing capacity test (A). The patient breathes through the mouthpiece (MP). Initially, the breathing valve (BV) is turned so that all breathing is in from and out to the room. After the patient exhales to RV, the breathing valve is turned to attach the patient to the spirometer filled with test gas containing carbon monoxide and helium. The patient inspires rapidly to TLC, breath-holds for ten seconds, and exhales rapidly. The breathing valve is left connected to the spirometer for the initial portion of this expiration, allowing the spirometer to record the amount of gas "washing out" the dead space. After the dead space has been flushed, the breathing valve is turned so that an alveolar sample is collected in the sample bag (SB). Gas analyzers measure the inspired gas concentrations from the spirometer, and the expired gas concentrations from the sample bag. A representative spirometer tracing is shown on the right (B).

CO content. The initial alveolar concentration of CO is not the inspired concentration, as the inspired gas is diluted with gas remaining in the lung prior to inspiration (the RV). In order to assess this dilutional reduction in CO concentration (as contrasted with the subsequent diffusive reduction), an inert gas that is readily diluted but does not diffuse or dissolve is added to the inspired gas. Suitable tracer gases for this purpose include helium, methane, and neon. The concentration drop of the tracer gas from beginning to end of breath holding is used to calculate the initial CO alveolar concentration as follows:

$$F_{ACOi} = F_{iCO} * \frac{F_{ETR}}{F_{iTR}} \quad (9)$$

where F_A =fractional concentration in alveolar gas

F_I =fractional concentration in inspired gas

F_e =fractional concentration in expired gas

CO =carbon monoxide

TR =tracer gas

Over the period of breath holding, the alveolar concentration of CO falls exponentially according to its partial pressure gradient between the gas and blood sides of the alveolar membrane (it is assumed that the blood concentration of CO is zero throughout the short breath hold). Then, the DLCO is calculated as

$$DLCO = V_I * \frac{F_{iTR}}{F_{ETR}} * \frac{1}{T} * \frac{1}{BP - 47} * \ln(\frac{F_{ACOi}}{F_{ECO}}) \quad (10)$$

where V_I =volume of inspired gas (sometimes adjusted by an estimate of dead space)

T =duration of breath hold

BP =ambient barometric pressure

and other parameters are as defined above.

The equipment needed to calculate the DLCO includes either a spirometer or a flow sensor to measure the inspired volume and gas analyzers to measure the concentrations of CO and the tracer gas. In some systems, the sample of expired alveolar gas is collected in a bag for analysis; in other systems with rapidly responding analyzers, the expired gas is sampled continuously for calculation. It is worth noting that using a flow sensor for this test requires that the flow sensor be calibrated with the gases to be used, as described above.

The DLCO is very sensitive for lung abnormalities but is also quite non-specific. Several conditions can cause marked reductions in DLCO, including emphysema and pulmonary fibrosis. DLCO can be increased in some cases of early heart failure and in cases of pulmonary hemorrhage. DLCO is reported at STPD conditions.

Lung Volumes

There are several different methods available for measuring the TLC, RV, and FRC. These parameters, regardless of how they are measured, are reported at BTPS conditions.

In the *helium dilution* method, a two-port spirometer is connected with tubes to a breathing valve and a blower motor. The spirometer is filled with a known concentration of helium and the patient, with no helium in the lungs, is attached at FRC by turning the breathing valve. At the beginning of the test, the total amount of helium contained within the system is equal to the initial concentration times the system volume. After 3-7 minutes of rebreathing, when the helium has been distributed evenly between the patient's lungs and the system, the final helium concentration is recorded [Fig. 15]. Then, owing to the fact that helium is inert and does not leave the lung via solution in tissues nor diffusion into the blood,

$$FRC = V_S * \frac{F_{HEI} - F_{HEF}}{F_{HEF}} \qquad (11)$$

where V_S =system volume

F_{HEI} =initial helium concentration

F_{HEF} =final helium concentration

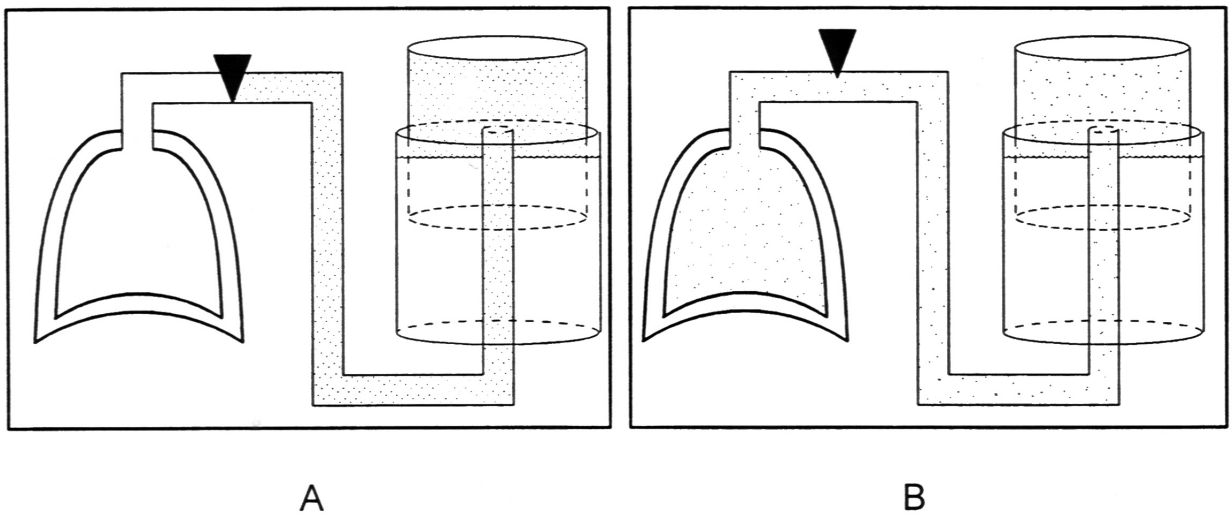

Figure 15. Diagram illustrating the helium-dilution lung volume test. Prior to the test (A), the spirometer system is filled with a known concentration of helium. When the test is completed (B) after the helium has distributed and reached equilibrium with the gas in the lungs, the ratio of final to initial concentration of helium is equal to the ratio of spirometer volume to spirometer plus lung volume. In practice, the spirometer used generally has two ports, not only one as pictured, and allows for better mixing of the gases (see text).

This test requires that some of the gas be circulated through a CO_2 removal canister to prevent exhaled CO_2 from rising to uncomfortable or dangerous levels during the rebreathing period. Oxygen is added periodically to maintain a constant total system volume at end expiration. Once FRC is obtained, TLC and RV may be calculated, after the patient performs one or more VC maneuvers, as described earlier. The helium dilution system, since it is a closed-system test, is almost always performed using a volume displacement spirometer. It also requires the use of a helium analyzer.

The *nitrogen washout* method attempts to "wash out" all of the nitrogen from the lung during a period of 100% oxygen breathing [Fig. 16]. All of the exhaled gas is analyzed for volume and N_2 concentration, which is integrated to give the total volume of nitrogen washed from the lung. By assuming a known initial concentration of nitrogen within the lung, and its volume, the total volume of gas contained within the lung may be calculated as follows:

$$FRC = \frac{V_{EN2}}{F_{AN2}} \tag{12}$$

where V_{EN2} =the total volume of exhaled N_2

F_{AN2} =the initial alveolar N_2 concentration (typically taken to be ~0.79)

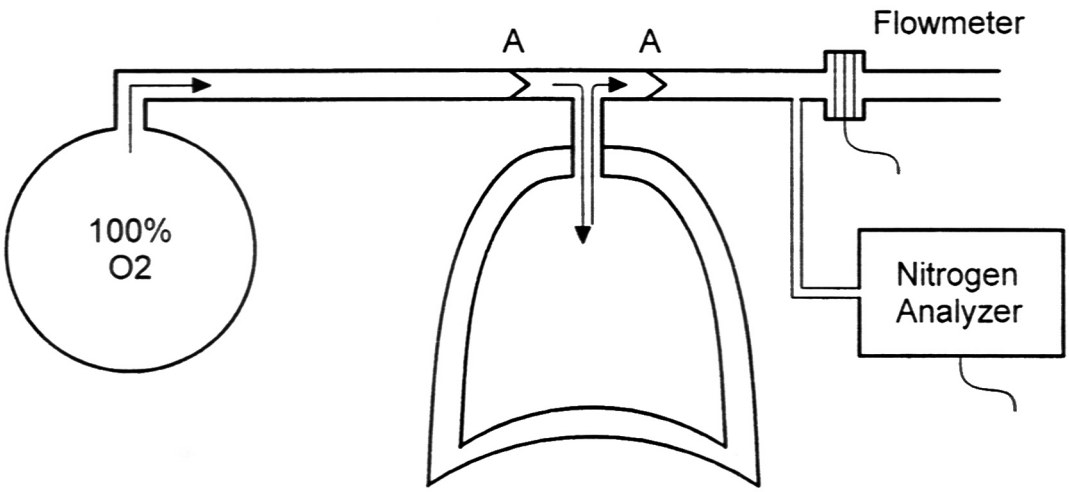

Figure 16. Equipment setup for a nitrogen-washout lung volume test. The one-way valves (A) keep separate the inspired and expired gas streams, as shown by the directional arrows. The total volume of nitrogen exhaled is calculated by integrating the continuous expired nitrogen concentration over the volume signal, which is in turn generated by integrating the flow signal over time. The nitrogen analyzer is also used to determine when the test is over, as indicated by an expired nitrogen concentration close to zero following the replacement of all lung nitrogen by other gases (oxygen and carbon dioxide).

The total volume of exhaled N_2 may be calculated by collecting all the expired gas in a very large spirometer and making a single measurement of its nitrogen concentration, or the expired gas may be analyzed continuously for N_2 content with simultaneous use of a flow sensor. Even

when the expired gas is collected separately, a continuous N_2 signal is helpful to detect leaks in the system that will interfere with accuracy.

Both the helium dilution and nitrogen washout tests also give information about the distribution of gas within the lung, as both will yield a curve closely following exponential decay when the helium concentration or the end-expiratory nitrogen concentration is plotted against time. Although this information may be useful in describing gas mixing within the lung, it has not been widely used in clinical practice.

A third method for measuring lung volumes uses a device known as a *body plethysmograph*, also referred to as a "body box." The body box is a large rigid-walled structure in which the patient is seated, after which the door is closed and sealed completely. In one variety, a small hole in the wall of the cabinet leads to a spirometer or flow sensor. Respiratory efforts within the box causes changes in volume to be recorded on this spirometer as chest wall movement displaces air within the box. In a second variety of body box, there is no hole in the wall of the box and respiratory efforts instead cause pressure swings within the box. At FRC, a valve at the patient's mouth is closed and the patient is instructed to pant. The rhythmic respiratory efforts cause rises and falls in both alveolar pressure (measured at the mouth) and opposite pressure or volume swings in the box around the patient [Fig. 17]. According to Boyle's Law, the product of the volume being compressed and its pressure remains constant. Thus

$$FRC * P = (FRC - \Delta V) * (P + \Delta P) \qquad (13)$$

where P =pressure measured at the mouth at the beginning of a pant

ΔV =change in lung volume due to compression during a single pant

ΔP =change in pressure at the mouth during a single pant

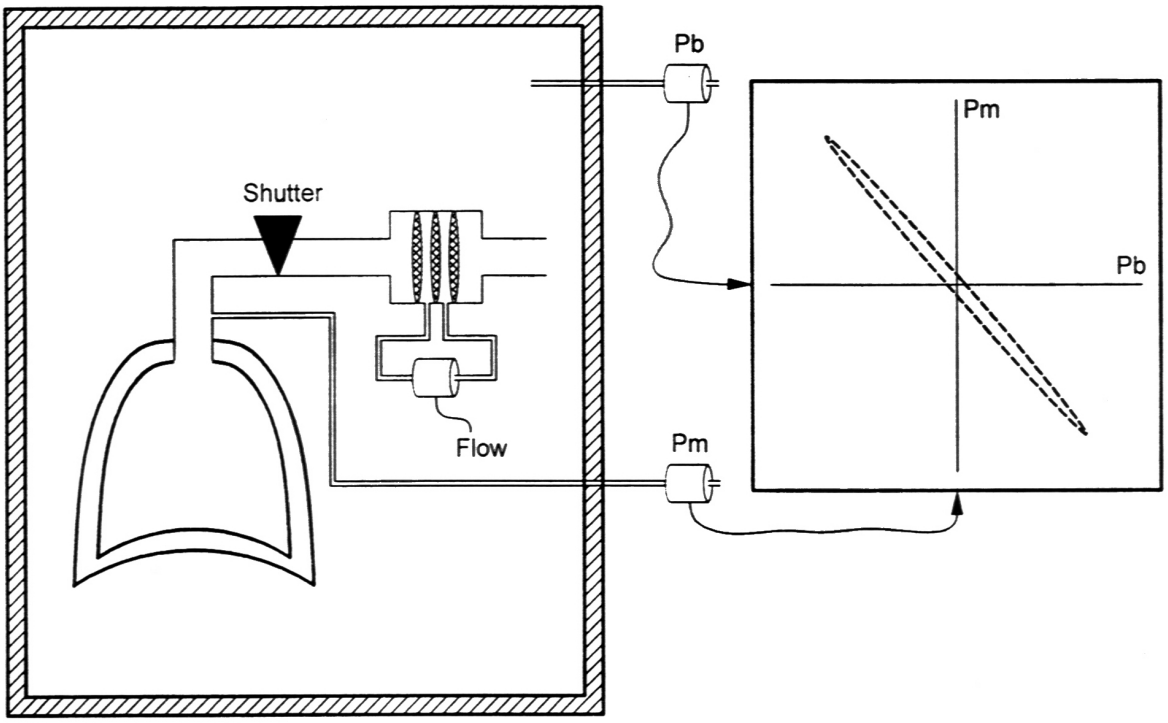

Figure 17. Illustration of a body plethysmograph, or "body box." The patient sits within the sealed rigid-walled box. For measurements of lung volumes, the patient pants against the closed shutter while box pressure (Pb) and mouth pressure (Pm) are recorded as shown. The slope of the relationship between Pb and Pm determines the volume of gas being compressed within the lung. For measurements of airways resistance, the shutter is then opened and an additional recording is made, this time with flow rather than Pm on the y-axis (see text).

The ΔV is measured either from the change in volume through the port in the side of the box, or by calibrating changes in box pressure to volume changes. The body plethysmograph allows for rapid multiple determinations of lung volume. It requires the large rigid box, one or two pressure transducers, and possibly a flow sensor or spirometer.

Airways Resistance

Measurements of airways resistance generally assume that Ohm's Law applies and therefore that

$$P_A = \dot{V} * R_{aw} \tag{14}$$

where P_A =alveolar pressure (measured relative to atmospheric pressure)

$\dot{V}$ =flow

R_{aw} =airways resistance

One method uses a body plethysmograph with a pneumotachograph at the mouth [Fig. 17]. It repeats the measurements described above in the discussion of lung volumes, and adds a series of pants with the mouthpiece valve <u>open</u>, allowing for airflow. During open-valve panting, the slope of the relationship between airflow at the mouth and changes in box pressure is recorded. During closed-valve panting, the slope of the relationship between changes in alveolar pressure and changes in box pressure is recorded. The ratio of these two measurements yields the airways resistance as follows:

$$\frac{\text{Closed Valve}}{\text{Open Valve}} = \frac{P_A / P_{Box}}{\dot{V} / P_{Box}} = \frac{P_A}{\dot{V}} = R_{aw} \tag{15}$$

where P_{Box} =pressure within the box

and other symbols as shown above

A second, non-plethysmographic technique for measuring airways resistance makes use of an airflow perturbation device (APD) [Fig. 18]. In this approach, the patient breathes through a mouthpiece connected to a flow sensor. A pressure transducer measures the pressure at the mouth. At the outlet of the flow sensor is a rapidly rotating wheel that intermittently creates a partial obstruction to airflow. During the time that there is no obstruction, the airflow is described by

$$P_A = \dot{V}_{open} * (R_{aw} + R_{open}) \tag{16}$$

$$R_{open} = \frac{P_{m,\,open}}{\dot{V}_{open}} \tag{17}$$

where P_A =alveolar pressure (relative to atmospheric)

$\dot{V}_{open}$ =flow with no obstruction

R_{aw} =airways resistance

R_{open} =resistance of the flow sensor and the device with no obstruction

$P_{m,open}$ =mouth pressure with no obstruction

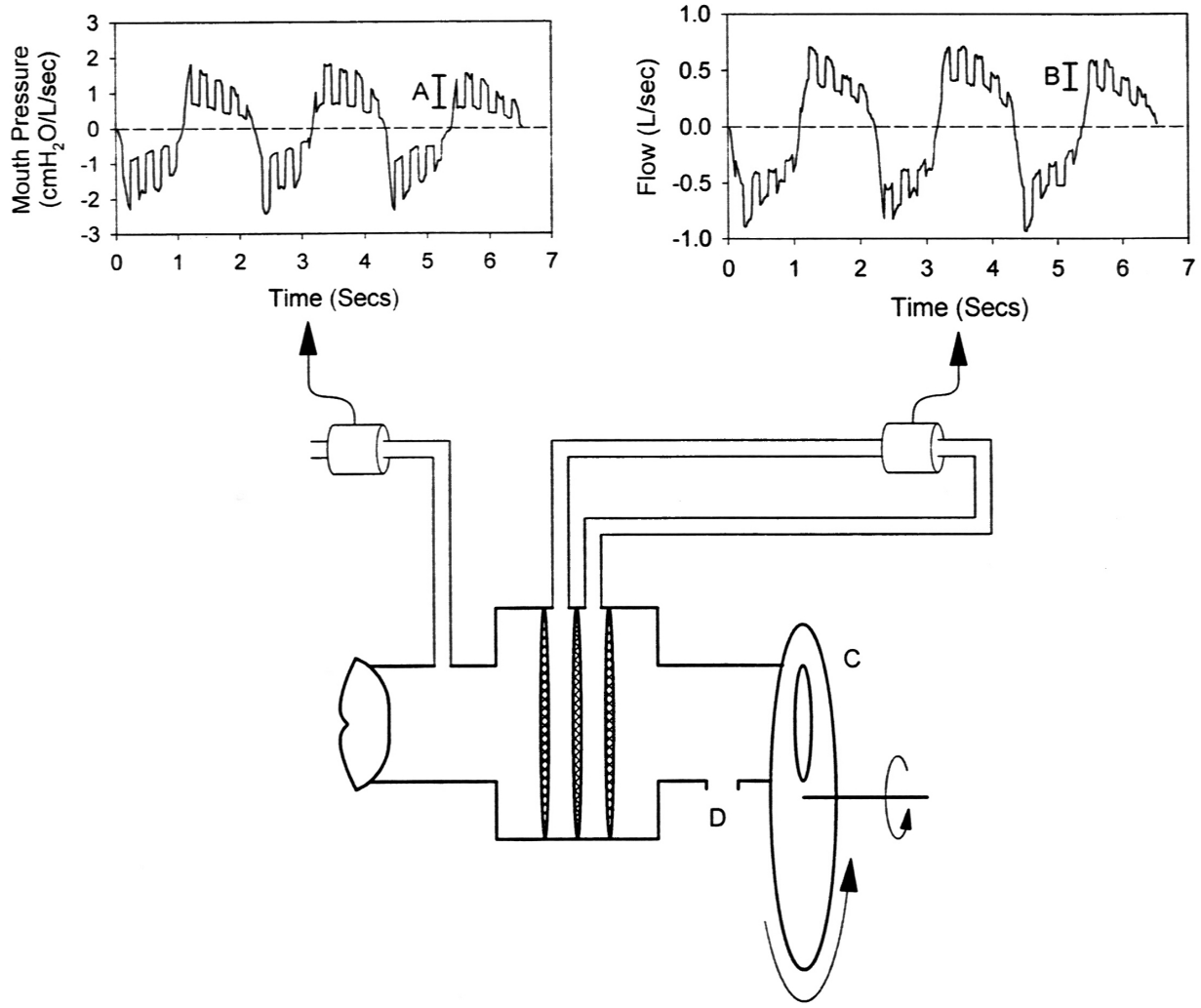

Figure 18. Diagram of the airflow perturbation device (APD). The rotating disk (C) creates changes in resistance through which the patient breathes. The ratio of delta-pressure (A) to delta-flow (B) with the partial obstructions is equal to the patient's airways resistance. The side opening (D) provides a flow outlet for periods when the rotating disk obstructs the outlet of the flow sensor.

When there is a partial obstruction, airflow is described by

$$P_A = \dot{V}_{obs} * (R_{aw} + R_{obs}) \tag{18}$$

$$R_{obs} = \frac{P_{m,\,obs}}{\dot{V}_{obs}} \tag{19}$$

where $\dot{V}_{obs}$ =flow with a partial obstruction

R_{obs} =resistance of the flow sensor and the device with a partial obstruction

$P_{m,obs}$ =mouth pressure with a partial obstruction

If the wheel spins rapidly enough so that each partial obstruction is short, the alveolar pressure is assumed to remain constant. Solving these equations yields

$$\text{Raw} = \frac{P_{m,\,obs} - P_{m,\,open}}{\dot{V}_{open} - \dot{V}_{obs}} = \frac{\Delta P}{-\Delta \dot{V}} \tag{20}$$

Oxygen Consumption and Carbon Dioxide Production

The simplest method for measuring carbon dioxide production ($\dot{V}_{CO2}$) is to collect a timed sample of expired gas in a balloon or spirometer, measuring the total volume of gas collected and its CO_2 concentration. If the inspired gas is assumed to contain no CO_2 (a reasonable assumption for most measurement purposes), then all of the CO_2 contained within the expired gas came from the $\dot{V}_{CO2,\,which}$ may be calculated as

$$\dot{V}_{CO2} = \frac{V * F_{ECO2}}{\text{Time}} \tag{21}$$

Unfortunately, a similar equation does not hold for measurements of $\dot{V}_{O2}$. The reason for this is that the inspired gas does contain oxygen, and thus there must be included a term to account for the fact that the oxygen consumed is the relatively small difference between the large amounts of total oxygen inspired and expired. Thus, an equation for $\dot{V}_{O2}$ is

$$\dot{V}_{O2} = \dot{V}i * F_{IO2} - \dot{V}e * F_{EO2} \tag{22}$$

where $\dot{V}e$ = average inspiratory ventilation in liters per minute

$\dot{V}i$ = average expiratory ventilation in liters per minute

And F_{IO2} and F_{EO2} are the inspired and expired oxygen concentrations, respectively

Note that, as described earlier, the $\dot{V}_{O2}$ does not ordinarily equal the $\dot{V}_{CO2}$, which means as a consequence that $\dot{V}e$ does not equal $\dot{V}i$. Some devices do measure separately the $\dot{V}e$ and the $\dot{V}i$, either with two flow sensors or a single flow sensor measuring in both directions (inspiration and expiration). However, it is possible to obtain a reasonably accurate calculation of $\dot{V}_{O2}$ by noting that, in the steady state, there is no net consumption nor production of N_2. Thus, the following equation for N_2 consumption may be set to zero:

$$\dot{V}_{N2} = \dot{V}i * F_{IN2} - \dot{V}e * F_{EN2} = 0 \tag{23}$$

Solving this for $\dot{V}i$ yields

$$\dot{V}i = \dot{V}e * \frac{F_{EN2}}{F_{IN2}} \tag{24}$$

Both F_{EN2} and F_{IN2} are known, so long as inspired concentrations of oxygen and carbon dioxide are known and no other gases (besides water vapor) are present, as follows:

$$F_{IN2} = 1 - F_{IO2} - F_{ICO2} \tag{25}$$

$$F_{EN2} = 1 - F_{EO2} - F_{ECO2} \tag{26}$$

Thus, combining these equations, $\dot{V}_{O2}$ may be calculated as follows:

$$\dot{V}_{O2} = \dot{V}e * \left[\frac{1 - F_{EO2} - F_{ECO2}}{1 - F_{IO2} - F_{ICO2}}\right] * F_{IO2} - \dot{V}e * F_{EO2} \tag{27}$$

Measurements of $\dot{V}_{O2}$ and $\dot{V}_{CO2}$, while possible with balloons ("Douglas bags") or large spirometers, is more commonly performed with a flow sensor and continuous O_2 and CO_2 sampling.

Other Devices

It is not possible in this space to describe all respiratory measurements and devices. However, those that have been described do represent some of those most commonly encountered in routine clinical and research applications. Commercially available systems, complete with software and printers, make easy work of performing these common measurements in the usual manner, and are constructed with components as described above. Often, however, these systems are ill-suited to making measurements that differ from common practice, even only slightly, without modification, if at all.

Design of Respiratory Devices

The designer of respiratory devices is, in many ways, faced with the same challenges as with other medical devices. There are many different aspects to consider, with device function being but one of these. In addition to device performance, there are safety, user interface, legal, biocompatibility, marketing, cost, and adaptability issues to face.

Concurrent Engineering

Modern engineering design methods often employ concurrent engineering, wherein designs are the result of teams of people representing various specialties working together toward a common goal. Especially for larger projects, teams may be formed from design engineers, marketing specialists, manufacturing engineers, packaging specialists, legal and regulatory specialists, servicing specialists, and others. Their common goal is to design an acceptable product in the shortest possible time for the smallest cost.

Before the adoption of concurrent engineering practices, each of these functions occurred in sequence: the marketing specialist surveyed past and potential users to determine what people liked and didn't like about prior models from this firm and from the competition; design engineers used computer model methods to create a new basic design; packaging specialists worked to create an attractive instrument that functioned according to user expectations; manufacturing people took this instrument and developed the means to mass-produce it and the quality assurance tests to be sure that each device met or exceeded minimum standards; the legal and regulatory specialists developed the data to meet government requirements in the country of use; sales personnel found potential users, compared the new device with the competition, and adapted the device to specific user needs; then the servicing specialists responded to customer concerns by developing quick field tests, parts kits, and field manuals to repair defective devices on site.

This procedure was time consuming and expensive. If the manufacturing engineer found that the

device could not be produced effectively as designed, then the whole design process had to be revisited. The same holds true for other steps in the process. There are legends about instruments that would not function without failure and that could not be serviced economically. The results were very expensive calamities.

Simultaneously considering all of these design aspects shortens the design process and allows industry to respond much quicker to customer needs or technological break-throughs. What once took 5-10 years to develop can now be done in one year or less. Perhaps because of this, attention has turned to regulatory delays for device approval, which are now an unproportionately large amount of time.

Small projects by small companies may not use formal concurrent engineering teams in the way that large projects in large companies require their use. However, the same functions need to be represented in the same parallel way. Because many medical devices are produced by small companies with few employees, the design engineer working for one of these companies must be able to wear many hats.

Technical Design

Design of medical devices employs a combination of fundamental engineering principles and empirical data. Almost all respiratory devices incorporate the need to move air from one place to another. At the least, it is usually desired to reduce airflow resistance and dead volume of the air circuit. There is no substitute for a thorough knowledge of fluid mechanics in order to realize

these goals. Minimizing the number of sharp bends, sudden constrictions, and obstructions can reduce resistance; reducing turbulence, tubing length, and compliant members can reduce dead volume. This knowledge comes from engineering principles and can be predicted beforehand.

A field as mature as the field of respiratory devices develops around a great deal of empirical knowledge. This information could, perhaps, be predicted from first principles, but often is determined by experimental measurement on previous devices or on prototypes of newly developed devices. Two devices where empirical knowledge is important are the body plethysmograph and the hospital ventilator. Each of these is a complex device that has undergone many embodiments over the years; each has been required to become more accurate or more versatile; each has been improved through knowledge gained by use.

The design process, then, is to begin a new device from basic engineering considerations and to make improvements based more and more on empirical information. Computer-aided design (CAD) and computer-aided manufacturing (CAM) programs are often constructed to incorporate the state of knowledge in compact and easily-used form. This has the advantage of allowing the information base to be constantly accessible without dependence on the memories of any particular individual. This makes these proprietary computer programs some of the most valuable assets of any company, and gives companies that have been manufacturing the same kind of medical device for many iterations an almost insurmountable advantage over younger companies that attempt to improve the same kind of device. Thus, newer companies are usually found developing newer kinds of devices that do not require as much empirical knowledge to produce. When these newer companies develop substantial amounts of their own empirical

technical knowledge, they become valuable for their technical information bases, and they become acquisition targets by larger companies wishing to develop their own devices of that type.

Safety

Most respiratory devices are noninvasive, which reduces the safety burden somewhat because there is no direct route for introduction of microbes into the interior of the body as with other types of devices. One of the main causes for safety concern is due to saliva: this fluid could be the pathway for stray electrical currents to enter the body. Even more important is the transmission of respiratory diseases.

Saliva contains a mixture of ionic substances and can conduct electricity. For this reason, there can be no direct electrical pathway from the ac supply to the patient. Thus use of isolation transformers should be seriously considered, especially when young children are to be measured. An alternative is the use of battery-powered units, which are especially attractive because there cannot be a stray path to ac electrical ground as long as the unit is not hooked to an ac electrical outlet. Although most hospitals have grounded ac outlets and ground fault interrupters, respiratory medical devices are being used in homes, clinics, and schools where such safety precautions may not be installed.

Saliva can carry disease organisms. To minimize the transmission of disease, disposable cardboard mouthpieces are used with many respiratory measurement devices. Respiratory

devices should, if possible, be designed to include sterilizable parts in the airflow path. This would reduce the possibility that microbes hitchhiking on aerosol particles would be passed from patient to patient.

Some ventilators and pulmonary function equipment for diffusing capacity can connect to cylinders of gas, the ventilators to supplemental oxygen, and diffusing capacity instruments to carbon monoxide. Connectors for gas cylinders of different gases are different to prevent accidentally connecting to the wrong kind of gas. If a mistake is made, asphyxiation is the result. Be sure to use the correct connector.

Costs

The range of costs for pulmonary function equipment is from less than $100 for home spirometers to $50,000 for hospital body plethysmographs. The cost must be appropriate for the use. In general, home use devices are much less costly then hospital devices. Home devices are usually much simpler and may not be as accurate or reliable as hospital devices. The design engineer must know the market for a new device before investing inordinate amounts of time or before including too many options that lead to inappropriate purchase prices.

Much of the cost of a new medical device is incurred due to governmental regulatory requirements. There is no practical solution to this because approval to manufacture requires amounts of device details and human trials to assure that the device is safe and effective.

Materials

Many of the materials incorporated in respiratory medical devices do not directly contact the person using the device. Therefore, materials are not subject to the same biocompatibility constraints as are implantable or surface contact devices. There is a need, however, to be sure that materials are rugged enough to stand up to repeated use under sometimes frantic circumstances. An endotracheal tube, for instance, must not fail during insertion into the trachea. In addition, materials in the air passage cannot give off toxic gases or undesirable odors or flavors.

Legal Liability

All medical devices are possible sources for legal action. Misuse or malfunctioning of the device can bring tort claims against the hospital, the owner of rented equipment, and the company of manufacture. The design of respiratory medical devices must design the device to minimize accidental misuse by the user by making the device as foolproof as possible, especially during emergency situations where the attention is on the patient and not the device. The manufacturer cannot be found to be negligent, or the manufacturer may be forced into severe penalties.

Optional Functions

There is a tendency on the part of a designer to incorporate many additional functions to give the device additional capabilities. There are cases where this is counterproductive, especially if the

complexity of device use increases beyond the point where mistakes can be made. Increasing the number of options often shifts the burden for a measurement from the device to the nurse or technician. Especially if these options are rarely used, they may not be useful even if they are appealing to the designer and marketing specialists. If options are to be included, make them hierarchical: the most important functions should be obtained with little effort by the user. Additional functions can be accessed with extra effort. For instance, the display on a computerized pulmonary function device should not show all possible measurements made with the device; only the one to three most important measurements should be displayed. Additional values, tables, or graphs can be displayed with additional switches, knobs, or touching the screen. Keep it simple.

Calibration

All hospital equipment requires periodic calibration to assure accurate measurements. Automatic calibration features allow for quick calibration at the point of use. If the instrument can self-calibrate, even for just the most important points, then it will be much more useful than if it must be moved to a shop for calibration. Some instruments undergo self-calibration when they are turned on. Other instruments are normally always powered, and can be calibrated either by pressing a button or by a timer (although this may interfere with a measurement). More thorough calibrations still need to be completed in a biomedical maintenance laboratory.

If the device has a linear input-output response, then there are normally only two calibration points, one at the device zero (null input), and the other at the span value (maximum input). It is

not uncommon that significant drift occurs in the zero value alone; it is not so common that the span value drifts independent of the zero value. That is fortunate, because a null input is easier to calibrate than is a span input. The instrument can be made to measure the output for null input and correct all readings accordingly.

Calibration of the device should be an important consideration when the product is being designed.

Human Factors Issues

Human factors considerations can be easily overlooked in the initial design of a medical instrument, which can result in the need for costly redesigns and delays in testing and approval. In these days when concurrent engineering practices are being applied to designs of everything from light bulbs to automobiles, it is important for the biomedical engineer to understand the medical environment in which the device is to be used. Especially important is to understand the various expectations for the device from personnel involved in its use.

The Patient

There is not one stereotypical patient, but several. One of these is a normal, healthy individual who is undergoing a routine physical examination. This examination might be for school, for personal reasons, or for work. There may be some apprehension exhibited by the patient when confronted by medical surroundings. Especially with a new medical device or test, the patient

will wonder what it will do to him or her. The patient will likely exhibit slight hyperventilation, her/his respiratory system may not be entirely normal, and the operation of the device can be viewed with suspicion.

Another patient may enter the hospital with a severe pulmonary condition. She/he may suffer from extreme dyspnea, can be nearly unconscious, and may exhibit symptoms of panic. Movement to standard pulmonary function testing equipment may require too much exertion, and he or she may be too preoccupied to fully cooperate. Special breathing maneuvers may not be within his/her capabilities. The operation of the device must be fast and able to occur where he/she is located, and, unlike the first patient, the instrument offers hope, not a threat.

The Technician

The technician is highly trained, but not in the way an engineer is trained. The technician is oriented toward the patient, and can coax and cajole the best effort and the best measurements from the patient. The technician can also add consistency to the measurement, because he/she often adds a great deal of discrimination when it comes to deciding whether a measurement should be kept or repeated.

The technician does not coax and cajole instruments very well. Operation of the instrument is ideally automatic up to the point where a decision is made whether to repeat or not. Too many buttons or too many choices take too much attention away from the patient, which the technician may not like.

The Physician

The physician shoulders the ultimate responsibility for diagnosis and treatment. She/he is busy, and has little time to make a judgment. The medical device, like the technician, must do what she/he wants instead of the other way around. The physician must have confidence in both the technician and the device in order that she/he may quickly look at measurement results and make a determination of the problem in a short time. The device should give unequivocal results so that it supports, rather than contradicts, other experiential evidence that the physician is considering. The physician wants a new medical device that relates to other devices and methods she/he has used in the past. Once accepted by the physician, the assumption is made that the new medical device gives 100% accurate results. In reality, the device does not always need to be extremely accurate, but it must be consistent.

The Engineer

It is the engineer who knows each flaw in the measurement. She/he wants to be proud of the instrument, and wants it to be perfect. The engineer wishes to be appreciated for all the bits of creativity and insight that have been incorporated into the machine and is disappointed when these are not appreciated. Her/his tendency, in the face of a compromise between machine and patient, is to require more of the patient. This tendency must be resisted. The engineer must have faith in her/his abilities, patience with those in the medical profession, and careful in her/his approach. Above all, she/he must realize that the medical world is different from her/his own,

and that, while nothing can stand between medicine and a technique that it craves, there is no path more strewn with obstacles than the path toward acceptance of a new medical device.

Physical Characteristics

Aesthetic design is important for device acceptance. Many respiratory devices are relatively small, and smallness is a positive attribute. There was a time when the very size and massive appearance of a device connoted robustness, but styles change, and now the appearance of elegance is in vogue. The device must look clean, small, lightweight, and sanitary. Computer displays must have a similar appearance as popular computer programs of the day. The color of the device should be rather neutral instead of gaudy.

Most medical devices are accepted better if they are lightweight. Respiratory devices may be used in the home, and home may be located up several flights of stairs. Even hospital equipment must be moved for cleaning or storage, so lighter devices are appreciated. Portability is beneficial.

Medical devices should be quiet. They should not appear to be contraptions to nurses and technical staff, and they should not cause loss of confidence by patients. They should not add to the din of a hospital environment, especially during emergencies, when communications among health care professionals are most critical.

Devices must be rugged. They cannot break if they are to fall on the floor during a medical

emergency. They must be able to withstand fluids that are sometimes all around in a medical setting. They must be able to stand electrical surges, and they should operate when placed in unconventional orientations.

If they can be made to work correctly in dusty or dirty environments, or at extreme temperatures, then they can be used under severe field conditions. However, most medical devices are expected to be used in clean conditions at moderate temperatures. Such conditions prevail in most modern hospitals in the developed world. In third world countries or during combat, however, medical environments are not as well controlled.

Governmental Regulatory Requirement

The US Food and Drug Administration (FDA) is the main regulatory body for medical device approval in the USA. It is the job of the FDA to determine that a new medical device is both safe and effective. Each medical device must meet both criteria of safety (it can do no harm) and effectiveness (it must do what it is purported to do).

Most new medical devices must undergo a process of premarket notification. Certain Class I devices (see the FDA website at www.fda.gov) are exempt from this requirement. There are certain respiratory-related devices in the list of Class I devices, but, in general, they are ancillary to respiratory diagnostic measurement and health care.

If the medical device is intended to be used in a new way or is based on a fundamental scientific

technology different from other devices, then the approval process is extremely thorough and is called Premarket Approval (PMA). If the device can be justified as a minor modification of a device that has received prior FDA approval for manufacture, then it undergoes an abbreviated 501(k) approval process. Neither of these processes is a trivial step, and specialists are often employed just to guide the device through to approval.

Medical device approval processes in other countries may or may not be similar to the process in the U.S. Mutual Recognition Agreements may be negotiated between different governments to allow judgments by National Conformity Assessment Bodies to be accepted in other countries.

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