ASSOCIATION OF RESPIRATORY TECHNICIANS AND PHYSIOLOGISTS

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BREATH

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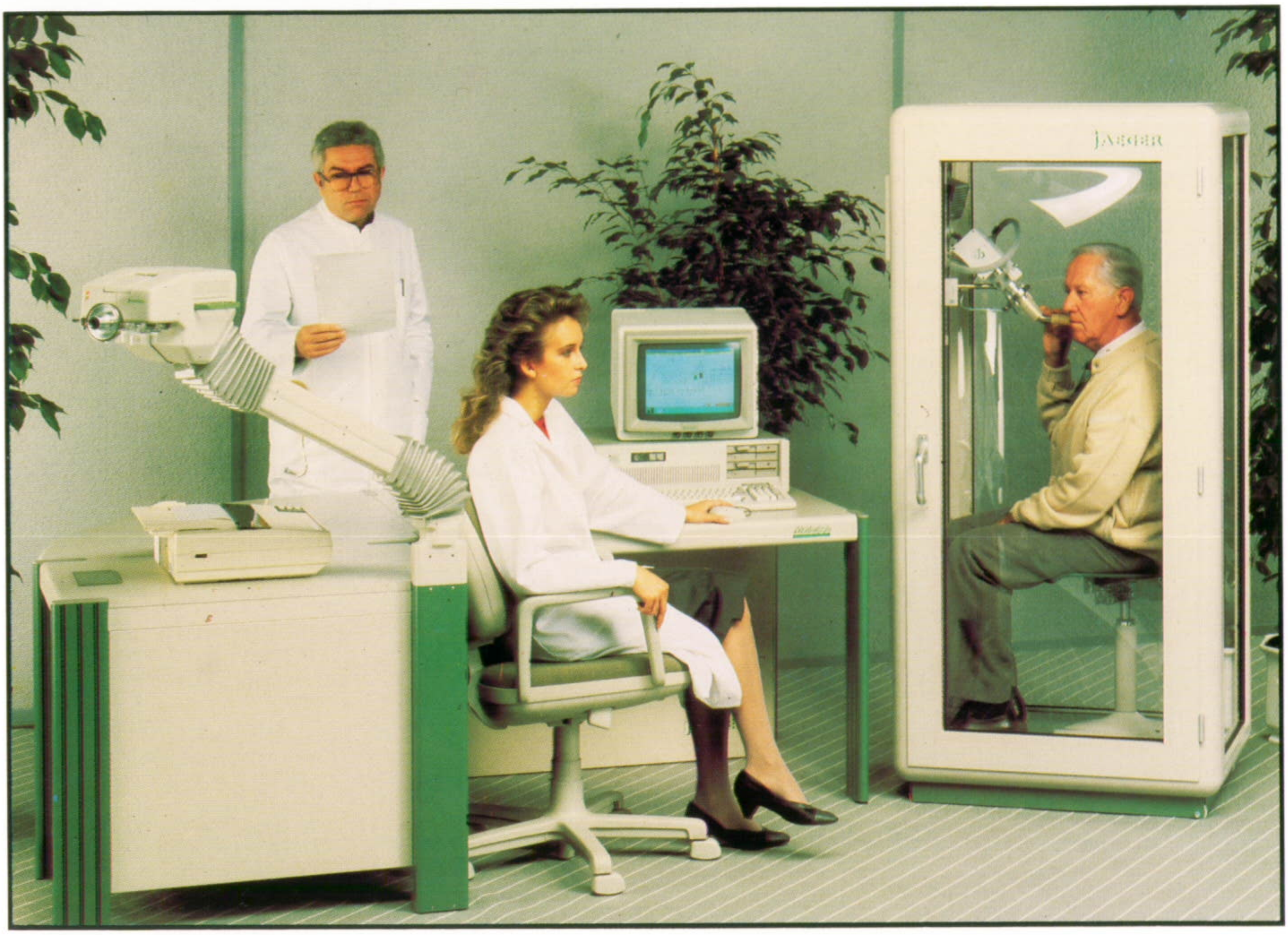

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- FRC-rebreathing
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Air is Our Life

The management of asthma - Where have we gone wrong?

Martyn Partridge

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Asthma is a potentially treatable condition and yet thousands still suffer because we have taken a 'sticking plaster' approach to the disease. All health professionals should take every opportunity to stress to patients with asthma that a safe future free of most symptoms is only achieved in the majority by the regular inhalation of anti-inflammatory therapies. Asthma is a life long condition in which risk and permanent lung damage are only avoided by proper treatment.

In the United Kingdom, as in most other developed countries, the problems of asthma are increasing. There is evidence of increasing rates of hospitalisation for patients with severe asthma, increased consultation rates in general practice and a continuing tragedy of over 2,000 patients with asthma dying from the disease every year. This epidemic of suffering is occurring despite the fact the prescription of anti-asthma drugs have also increased dramatically. How can this paradox of increasing suffering in the presence of increased therapies be explained? Unfortunately the answer is by no means clear but there are four possibilities:

1. The prevalence of the disease may be increasing.

If more people had the disease there would be greater need for anti-asthma prescriptions and, if the same proportion of asthmatics were dying, there would be numerically more deaths simply because there are more people with the disease. These possibilities would explain the persistent high and probably rising death rate, but it is a difficult area to study.

The evidence suggests that there are more people with the disease but some of this increase relates to more accurate diagnosis by doctors; thus many patients who might previously have been diagnosed as having 'wheezy bronchitis' or recurrent chest infections are being correctly diagnosed as having asthma. This increased diagnostic accuracy accounts for some but not all of the increased prevalence of asthma and it is likely that there is a genuine increase in the number of people with the disease. Why this should be is unclear but although we no longer suffer "smogs" there are many remaining invisible environmental pollutants which may be damaging respiratory epithelium and permitting easier entrance of allergens.

2. Medication may be harming the patients

The second possible explanation for increased suffering despite increased use of medication is the uncomfortable possibility that we are harming our patients. When death rate and rate of prescriptions rise in parallel it is absolutely correct that we explore this possibility. In the 1960's there was an epidemic of asthma deaths when patients were found dead at home clutching their inhalers. The latter at that time contained relatively strong doses of beta-agonists which were lesss specific in their effect on the airways, and could affect the heart. However, it is is unlikely that the drugs themselves were in fact the cause of the asthma deaths at that time and it is more likely that the introduction of readily available self treatments from inhalers led to patients staying at home and delaying the seeking of medical advice. The problem in the 1960's was therefore in part a failure of education of patients rather than their demise due to drugs.

More recently there has been an upsurge in the use of nebulised bronchodilators and many doctors are concerned that the home use of nebulisers by patients may again lead to a dangerous delay in patients seeking help. If patients are allowed home nebulisers they must be issued with clear guidlines as to safe usage. However, it is fair to say that no study has shown that increased usage of nebulised brochodilators either in the community or in hospital is responsible for the continued mortality from asthma. A recent evaluation of a rising death rate from asthma in New Zealand led to a scare regarding a posssible correlation with one particular bronchodilator therapy widely used in that country but the evidence for a connection between that drug and the increased mortality is speculative.

3. The disease may have become more severe.

Perhaps the explanation for increased suffering from asthma and a continued death rate lies with an increasing severity of the disease? Over the last decade or so an asthmatic has become 16% more likely to be admitted to hospital with acute asthma but in adults this is likely to be due to hospital being perceived as the correct place to be with severe asthma, rather than there being evidence that the attacks are more severe. However, that is not the case with children and in young children especially there is recent evidence to suggest that for unknown reasons the disease is becoming more severe.

4. Patients may not be receiving optional therapy.

The likeliest explanation for the paradox of a rising morbidity and mortality in the presence of increased prescriptions of anti-asthma drugs is that we are prescribing the wrong type of medication and that in the midst of plenty too many patients are being inappropriately or inadequately treated. There are essentially two types of asthma therapy -

relieving therapies (bronchodilators such as salbutamol and terbutaline)

and preventative anti-inflammatory therapies which have to be taken regularly to prevent symptoms, such as cromoglycate (Intal) and inhaled steroids (beclomethasone and budesonide - marketed as Becotide, Becloforte and Pulmicort). Only about 20% of anti-asthma prescriptions are for these preventative therapies and in patients with severe asthma requiring admission to hospital it was shown in one study that only 37% of the patients were taking preventative anti-inflammatory therapies. The very effectiveness of the bronchodilator treatments means that we may be taking a 'a sticking plaster approach' to asthma and taking the symptoms away but doing nothing about the underlying disease.

Why should we be using more regular preventative treatment? One of the cardinal features of asthma is that the patient has more irritable or twitchy airways than usual and when some trigger then comes along the patient suffers the all too familiar coughing, wheezing and breathlessness. There is a reasonably close correlation between the degree of this bronchial hyper-reactivity and variation in peak flow rate between morning and night and far too many asthmatics suffer nocturnal or early morning symptoms without complaining. These symptoms are a sign of poorly controlled asthma and risk and can be suppressed by regular inhaled steroids. Work from Finland and the UK has shown that even when the patient feels well and is free of symptoms the state of bronchial hyperreactivity persists and there are profound inflammatory changes occurring in the airways. Whilst this inflammation persists the patient is at risk of unexpected severe attack and if not suppressed and the asthma is left untreated, then the disease is likely to become fixed and unresponsive with time.

For all of these reasons we must move away from the sticking plaster approach to asthma and be much more aggressive in encouraging patients to take regular preventative therapies. In children this may be with cromoglycate (Intal) or with inhaled steroids, and in adults this will most certainly be with inhaled steroids. Delivered directly to the site of action these are used in small doses and whilst a risk versus benefit analysis must be performed with all prescribing, in standard doses these therapies are extremely safe and very effective.

The patients' fears about therapy and their expectations of treatment should be explored and discussed as they will only comply with therapy if they have a good understanding of the disease and the rationale behind the therapy. This information should be given verbally and reinforced by means of leaflets, posters, audio tapes and video tapes. Once the patient is in the position of having this core of information about their disease they should have that information personalised for them and should be given written advice about how to alter therapy under certain circumstances. This advice can relate to symptoms but it is better to relate therapy to an objective measurement and many patients benefit from home self-monitoring with peak flow recordings. They may then be given a self management plan as shown in table 1. These plans can be easily inserted on an excellent range of asthma cards for adults and children (with copies for school teachers) which are available free from the Asthma Society. If suffering is to be reduced all health professionals must help to spread the correct messages about the treatment of asthma. The National Asthma Campaign (the combined charity of the Asthma Society and Asthma Research Council) provides a wide range of leaflets about asthma, and provides asthma cards for patients. They can also loan videos about asthma and publish a newspaper (Asthma News) three times yearly with up to date information about the disease. Membership of the National Asthma Campaign costs £3.00 per annum and perhaps members of the ARTP would be willing to help by displaying leaflets on a notice board and having membership forms available. Of equal or greater importance is the need for ARTP members to help our patients understand that for most patients asthma is a life long condition which if not regularly suppressed will give rise to symptoms, risk of severe attack and risk of permanent lung damage.

Further information is available from

The National Asthma Campaign
(The combined charity of the Asthma Society and the Asthma Research Council)
300, Upper Street,
London, N1 2XX

EXAMPLE OF A SELF MANAGEMENT PLAN FOR A MAN OF 30 WITH ASTHMA

Your usual treatment is Becotide '100', 2 puffs twice a day **regularly** . If you suffer wheezing, coughing or shortness of breath, relief may be obtained by taking 2 puffs of your Salbutamol inhaler.

You should measure your peak flow rate regularly and especially if you have any symptoms.

Your usual peak flow will be around 500.

If your peak flow falls below 400
  increase the Becotide to 4 puffs twice a day
  and take Salbutamol, 2 puffs four times a day.

If you peak flow falls below 250
  start Prednisolone tablets, 40 mg. per day and continue until your peak flow is 450
  and then reduce to Prednisolone, 20 mg. daily for a further 5 days.

If your peak flow is ever below 150 contact Dr. Smith urgently or attend the nearest hospital emergency department.

Historical Development of the Gas Laws

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Introduction

The process of gaseous exchange of 0_2 in the lungs requires the gas to pass from alveolar air, across the alveolar-capillary membrane and into combination with haemoglobin. From here it is transported via the circulatory system to the regions of cellular respiration and back, via the circulation, to the lungs where CO_2 diffuses into the alveoli and thence is excreted into the atmosphere (figure 1).

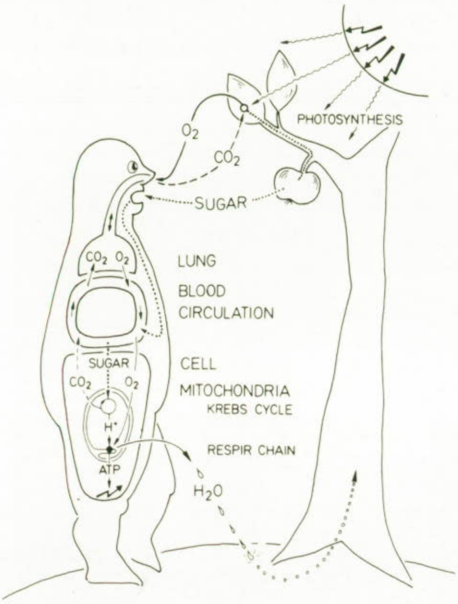

Figure 1. The oxygen cycle:- the energetic needs of our body are paid for by solar energy. Reprinted by permission of the publishers from THE PATHWAY FOR OXYGEN: Structure and Function in the Mammalian Respiratory System by Ewald R. Weibel, M.D., Cambridge, Mass.: Harvard University Press, Copyright © 1984 by the President and Fellows of Harvard College.

The various processes of gas exchange may be estimated in terms of the partial pressure of a gas or the rate of production or the rate of uptake of a given gas. To determine these indices, it is important to understand the fundamental laws of physics and chemistry applied to gas exchange. This will help to clarify the apparently confusing and perhaps illogical expressions that are used when expressing estimates of various indices.

This review will outline the historical development of the various laws of physics and chemistry and the equipment applicable to respiratory physiology. In a subsequent article the application of these laws to pulmonary gas exchange and other areas of respiratory measurement will be considered.

Development of Barometers and their Application

In the seventeenth century much activity centred around the experiments of Evangelista Torricelli (1608-1647) and his associates, who made the first barometer using mercury (1). It consisted of a long glass tube completely filled with mercury, which was then inverted into a dish of mercury. When inverted, the mercury fell, leaving a space at the top of the tube.

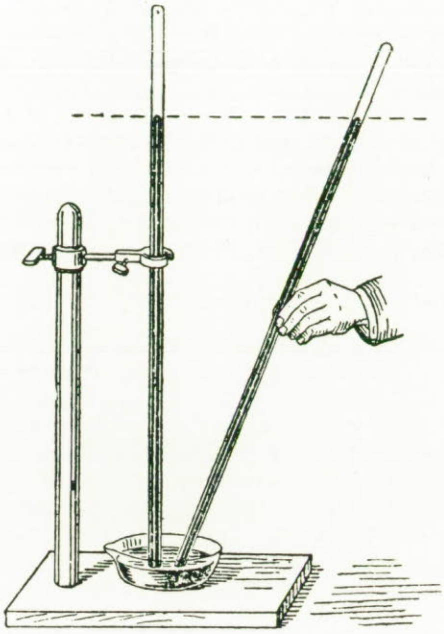

Figure 2. Classic Torricelli experiment: The height of the mercury level in mmHg gives an indication of the baromic pressure. When the tube is inclined to the vertical, the length of the tube occupied by the mercury will increase, but the vertical height above the surface in the resevoir will be unaltered.

Repeating the experiment with tubes of differing internal diameter did not affect the height of the mercury column. Much discussion centred around the interpretation of these findings. Some believed that the height of the mercury column was determind by the weight of the atmosphere pressing down on the surface of the mercury in the dish. Others were not so convinced!

The principle of Torricelli's findings is that the atmospheric pressure does indeed act downwards on the surface of the mercury, and since this is not balanced by the air pressure inside the tube, the mercury will rise in the tube until equilibrium is re-established. This equilibrium occurs when the downward pressure due to the weight of the mercury inside the tube exactly balances the upward pressure in the tube due to the atmosphere outside.

Blaise Pascal (1623-1662) considered Torricelli's findings and concluded that if indeed the height of the mercury column was determined by the weight of the atmosphere, then at high altitude, the height of the column should be less. To prove this, Pascal had a barometer taken up the Puy de Dome, a mountain of 1465m in the Massif Central, near Clermont-Ferrand, France. He confirmed his hypothesis and concluded that since the air "thins" as one ascends from the sea level, there is less pressure acting downwards on the mercury, so the level will fall. This simple application allows simple measurements of the height of mountains since as a rule of thumb, a fall of 2.54 cm on the barometer reading represents an alteration of about 274m in altitude.

Since Torricelli's experiment, the theory of mercury barometers has been greatly advanced (1). It is now recognised that the atmospheric pressure or absolute force per unit area is the product of three factors - the height of the mercury column, the density of the mercury and the acceleration due to gravity. Using these and other factors, it is possible to calculate the standard atmosphere (2). The standard atmosphere is a hypothetical atmosphere approximating to the average state of a real atmosphere in which pressure and temperature are 15°C at 760 mmHg. The pressure can be predicted for any altitude from 0 to 11 km above sea level (the troposphere). Barometric pressure (mmHg) may be calculated from this standard if the altitude above sea level is known (3). However, this standard does not reliably indicate mean barometric pressure. Mountains introduce variations in their immediate vicinity and air density and temperature vary from region to region over the surface of the earth.

The length of the measuring scale and the density of the mercury vary with the temperature of the barometer, whereas gravity varies with latitude. This variation occurs because of the flattening of the earth at the poles. The distance of its surface from its centre of gravity is least at the poles (polar radius - 6365km) and greatest at the equator (equatorial radius - 6378 km). Additionally, the vertical centrifugal force due to the earth's rotation is greatest at the equator and decreases to zero at the poles. The force of gravity therefore increases steadily from low to high altitude. Therefore theses factors must be standardized to specify the pressure in mmHg or Torr (named after Torricelli).

If the height of the column is to be read accurately, the barometer and its scale must be exactly vertical and the mecury surface in the reservoir must be adjusted to the zero of the scale. In the common precision instruments of the Fortin design (figure 3a) this zero setting is accomplished by adjusting the bottom of the mercury reservoir until the surface of the mercury in it is just barely in contact with the ivory tip, but without being dimpled by it (figure 3b). The level of the other surface, exposed to the Torricellian vacuum is then read by sighting across the highest point of the meniscus. A vernier device is commonly provided to read the scale to 0.1mm or 0.1 inch, without parallax (figure 3c).

Physiological effects, however, depend on the actual barometric pressure at the subject, which may be quite different from the value sited in the local weather report. If the barometer is at a different altitude from the physiological experiment such as on a different floor of a multistorey building, then a small altitude correction may be required. The International Civil Aviation Organisation "Standard Atmosphere" gives the likely difference in ambient pressure to be expected between the altitude of the barometer and that of the experiment (3). For a 3m difference, the correction would be −0.5 mmHg, whilst for a 50m difference the correction would be −4.5 mmHg. However, this correction only applies if the only cause of that pressure difference is the weight of the intervening column of air. If a ventilating fan or some other device contributes to the difference in pressure, then the correction cannot be used. Conversion tables are available for these corrections (4).

Details of the use of mercury barometers are available (5). One very important point about their use is the preservation of the Torricellian vacuum, especially when it is being moved. Failure to maintain this vacuum may lead to serious errors in the estimate of PB (6). If air is admitted or if the barometer needs cleaning, repairs should only be carried out by an expert. The processes in repairing and cleaning involved are both complex and potentially dangerous because of the toxic nature of mercury (5). Calibration should be carried out by a recognised organisation and a certificate obtained.

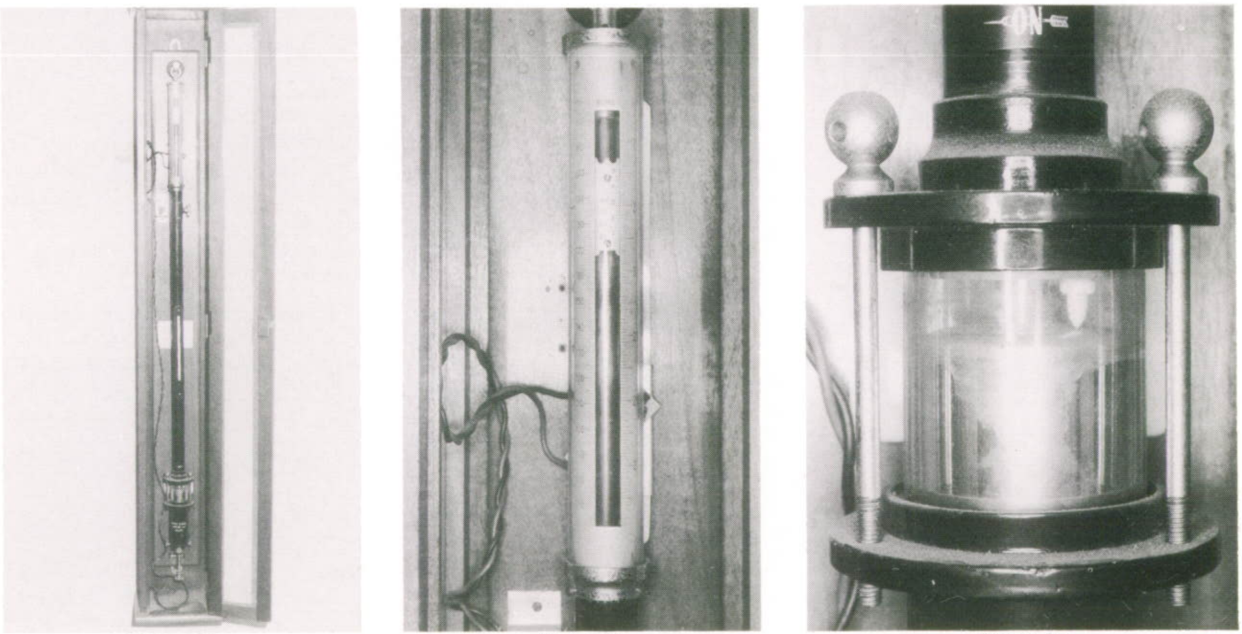

Figure 3a *Figure 3b* *Figure 3c*

Figure 3. Precision barometer of the Fortin design; a) the barometer, b) setting of the mercury reservoir, c) reading the barometer's pressure using the vernier scale.

Barometers used by the Meteorological Office must be corrected for the effects of temperature. Furthermore corrections must be made for the height of the barometer above sea level and the effects of gravity due to different latitudes (3).

Unlike meteorologists, physiologists do not need to carry out the complex corrections to reduce barometric pressure (PB) to sea level. Wind and weather are influenced by horizontal differences in the pressure gradients above the earth's surface. Meteorologists compare PB readings predicted for a single altitude of sea level on the assumption that the column existing between the barometer and sea level is occupied by air rather than solid ground.

Boyle's Law

Robert Boyle (1627-1691) used an improved version of von Guericke's (1602-1686) vacuum pump to establish whether it was atmospheric pressure that supported the mercury column of a barometer. By placing a pump inside a suitable vessel and pumping out some of the air, Boyle and Hooke (1635-1702) showed that it was the pressure of the air that supported the mercury column (7). Francis Linus (1595-1675) however disagreed with Boyle's work, believing that something invisible above the mercury held it up (8).

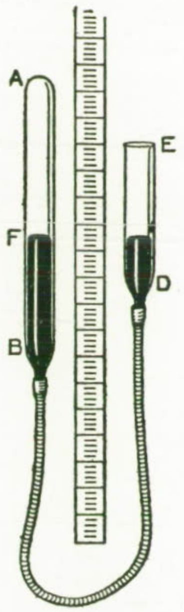

Figure 4a

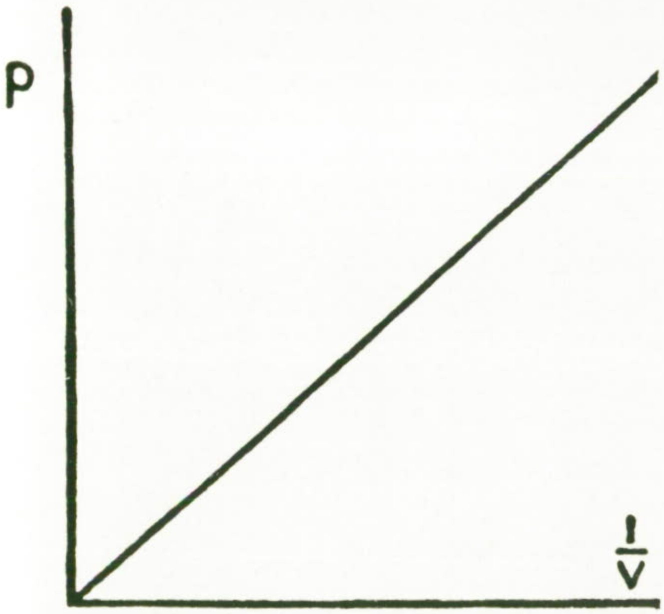

Figure 4b

Figure 4. Boyle's Law apparatus. a) AB is a glass tube of uniform bore closed at the upper end A. The lower end, which is open, is connected by means of rubber pressure tubing BD to a second glass tube open at both ends. The lower portions of the tubes AB and ED together with the whole of the pressure tubing are filled with dry clean mercury, whilst a suitable mass of air occupies the space above the mercury in tube AB. The tube AB is fixed in a vertical position, whils tube DE can slide up and down a vertical stand. A vertical scale serves to measure the heights of the mercury surfaces in the two tubes. To start the experiment, the levels of the mercury in the tubes AB and DE are set at equal heights, and therefore the volume of gas AF is at atmospheric pressure. Rasing tube ED will result in a difference in the levels of mercury in the two tubes and the pressure inside the closed tube will be greater than atmospheric. Thus, if h is the difference in level and P is the atmospheric pressure, the new pressure in AB will be $(P+h)$ *mmHg. The volume of gas in tube AF is calculated knowing the cross-sectional area of the tube and the length of gas contained in it. A number of readings above and below the starting point of the experiment are made and plotted as in b) which shows that P is proportional to 1/V.*

In defending his work, Boyle used the work of Henry Power (1623-1668) and Richard Towneley (1629-1706) who had put air above the mercury in a barometer and carried it up and down a hill. They concluded that the volume of the air changed inversely with pressure (9).

Boyle improved these experiments by making quantitative measurements of air trapped over mercury in a U-tube (figure 4a). When additional mercury was poured into the open end of the U-tube the volume of trapped air decreased in proportion to the increase in its absolute pressure (the sum of PB and the difference in the heights of the mercury in the arms of the U-tube). Conversely, when the pressure on the trapped air was reduced below atmospheric, its volume increased in proportion to the decrease in its absolute pressure (10). The relationship of volume to pressure is shown in figure 4b.

This establishes Boyle's Law, which states that

"at a constant temperature the volume (V) of a given mass of gas varies reciprocally with its absolute pressure (P)".

Thus PV is constant. (1)

It is important in stating Boyle's law to specify that the temperature of the gas remains constant since the volume of a given mass varies rapidly with temperature.

Charles's Law

The first attempt at investigating the effects of temperature on gas volume was reported by Guillaume Amontons (1663-1705) who wished to harness heat to move machinery. From his experiments he concluded that the temperature of water could not be raised above that at which it boiled; that unequal masses of air would increase their pressure equally when heated to the temperature of boiling water at a constant volume and that if allowed to expand at constant PB the volume of any given gas would increase in volume (11,12). This agreed with Boyle's law and the results are summarised graphically in figure 5.

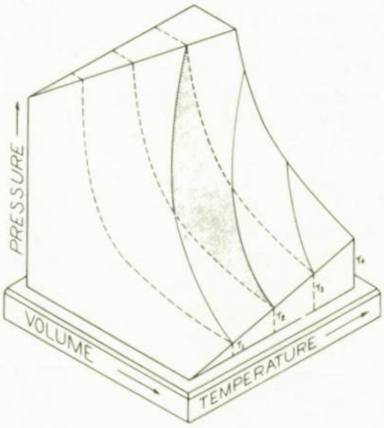

Figure 5a

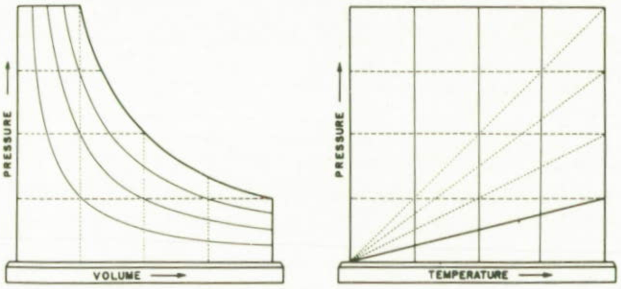

Figure 5b & 5c

Figure 5. P-V-T relationships for an ideal gas a) three dimensional plot showing the Carnot cycle as the shaded area. Two dimensional plots are shown in b) for pressure-volume and in c) for pressure temperature. The solid lines represent isothermal processes. (Reproduced with permission from Thermodynamics, Kinetic Theory, and Statistical Thermodynamics, by FW Sears & GL Salinger 3rd Ed, Addison Wesly, 1975).

These findings, obtained from meticulous experimentation by Amontons were disputed by many, principally because few subsequent investigators realised that to be consistent with the findings of Amontons, the gas had to be dry. Many investigators appeared to ignore the fact that if a gas is in contact with liquid water, heating the system not only expands the gas already present but adds an additional mass of gas due to evaporation from the liquid water.

John Louis Gay-Lussac (1778-1850) finally clarified the discrepancies. He realised the problems of water and ensured that as far as possible his gases were dry at all times. With these precautions all the gases tested followed the same quantitative law - expanding and contracting equally for equal increases and decreases in temperature (13).

About 15 years before Gay-Lussac's work, Jacques-Alexandre-Cesar Charles (1746-1823) had attempted similar experiments, but had never published the results. In writing up his own work, Gay-Lussac included reference to the work of Charles, noting some design faults in the latter's experimental apparatus leading to incorrect estimates for the coefficient of expansion of gases. The ironic twist to this is that the definitive work is commonly referred to as Charles's law rather than Gay-Lussac's law (so much for honesty!). In reality this is probably a good twist since Gay-Lussac's name is applied to the law of combining volumes - gases combine chemically in volumetric proportions (STPD) that are small whole numbers (14).

The ideal gas law which combines both Boyle's and Charles's law may be summarized by referring to the formulations used in the classic papers on thermodynamics. Sadi Carnot (1796-1832), in describing the Carnot cycle dealt with the effect of changing combinations of pressure and temperature on the volume of a fixed mass of gas in the sealed cylinder of an ideal engine (15). In essence this is a reversible cycle in which the working substance is compressed and expanded adiabatically (no heat enters or leaves the system) resulting in the pressure, volume and temperature returning to their initial values. This represents the cycle of an ideal heat engine.

Carnot combined the laws of Boyle and Charles by saying that

$$V = c\,(267+t)/P \qquad (2)$$

where V is the volume, t is the temperature in °C. P is pressure, c is a constant that depends on the weight of the gas and the units used, and 267 is the value to convert °C to Kelvin, this being the best estimate at that time (now 273K)

Equation of State

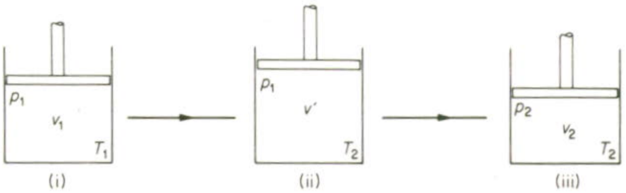

Figure 6. Effect of changing temperature and pressure of a gas. (Reproduced with permission from Advanced Level Physics, M Nelkon & P Parker, Heinemann Educational Books, 1977).

Figure 6 illustrates the arguments by which we may find the general relationship between pressure, volume and temperature for a given mass of gas. In figure 6i, a gas occupies a volume V_1 at a pressure P_1 and an absolute temperature (273+t), T_1. To calculate V_2 at an absolute temperature T_2 and a pressure P_2 we proceed via figure 6ii to figure 6iii.

In figure 6ii, T increases to T_2 and maintaining P_1 results in an increase in V to V'.

Therefore by Charles's law -

$$V'/V_1 = T_2/T_1 \qquad (3)$$

Proceeding to figure 6iii, the pressure is increased to P_2 whilst T_2 remains constant. Consequently V_2 decreases. By Boyle's law

$$V_2/V' = P_1/P_2 \qquad (4)$$

By rearranging and combining equations 3 and 4, we can say that

$$T_2V_1/T_1 = V' = V_2P_2/P_1 \qquad (5)$$

Emile Clapeyron (1799-1864) later defined all possible contributions of pressure and volume that might be derived from an internal combustion engine using the equation.

$$P_2V_2 = P_1V_1T_2/T_1 \qquad (6)$$

To simplify this equation, he proposed that

$$R = P_1V_1/T_1 \qquad (7)$$

and therefore equation 6 becomes

$$PV = RT \qquad (8)$$

which is the so-called "ideal gas equation" or "equation of state".

Rudolf Clausius (1822-1888) developed Clapeyron's work further, and noted that R varied from gas to gas in such a way as to be inversely proportional to the specific gravity. However, at any given pressure, volume and temperature -

$$\text{relative density } p = \text{mass/volume} \qquad (9)$$

$$= \text{molecular weight x mmols/unit volume} \qquad (10)$$

Johannes Diderick van der Waals (1837-1923) replaced R by nR where n is the number of moles, making R a universal gas constant, which is the same for all ideal gases. Thus equation 8 becomes -

$$PV = nRT \qquad (11)$$

Dalton's Law and the vapour pressure of water

If the mass of gas remains constant, then the laws of Boyle and of Charles (Gay-Lussac) are correct. When the gas equilibrates with liquid water, they do not hold true. Dalton's law of partial pressure and the effect of temperature on the vapour pressure of water must be used in this situation. Although readily accepted today, the ideas of Dalton's law could not be understood until the second half of the 18th century when it was realised that O_2, N_2 and CO_2 were different gases (16). However, it was not immediately obvious that these gases mixed physically rather than combining chemically with air.

Dalton (1766-1844), as professor of Mathematics and Natural History published his first book in 1793 entitled "Meteorological Observations and Essays" (17) in which he asserted that water was present in the atmosphere and was dispersed among the particles of other gases. He measured the partial pressure of water vapour as a function of temperature and the temperature of boiling water as a function of absolute pressure. He concluded that air takes up water physically rather than chemically, and that air takes up more water as temperature increases (figure 7).

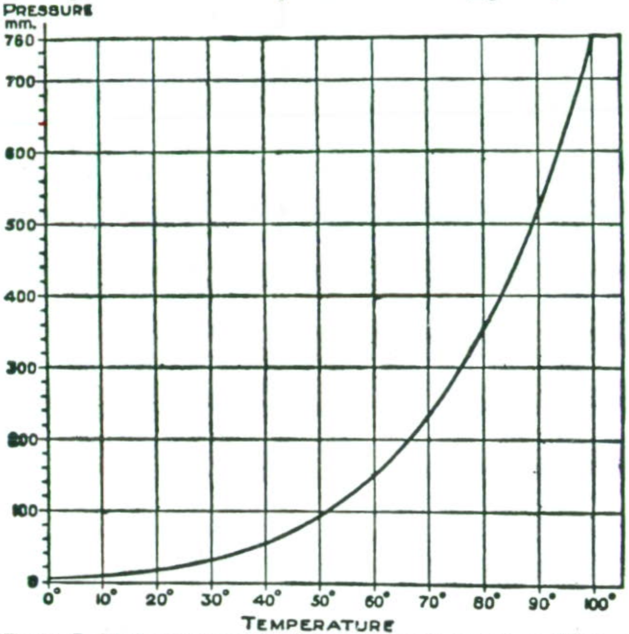

Figure 7. Maximum pressure of aqueous water vapour at different temperatures.

Dalton further presented his work in 1802 (18) at the Literary and Philosophical Society of Manchester. He spelled out his conviction that when two gases are mixed, there is a mutual repulsion amongst the particles; the particles of gas exert the same pressure as they would if the other were not present, and the total pressure is the sum of the partial pressures. He based his ideas of physical mixing on the fact that when different gases, such as O_2 and N_2 are mixed at constant pressure, the volume of the mixture equals the sum of the two initial volumes and there is no sign that they combine into a denser material of different chemical properties, such as happens when O_2 and NO combine to form NO_2. Although gases have different densities, there is no evidence to show that they layer when thoroughly mixed. Dalton also observed that when a liquid evaporated into a fixed volume of gas, the pressure increased by an amount determind by the temperature and therefore the vapour pressure of the liquid, and it was independant of the volume and pressure of the gas already present.

Dalton confirmed that dry gases followed Boyle's law, but noted that if atmospheric air saturated with water vapour was compressed, Boyle's law was not exactly followed since condensation of water vapour occurred to keep its partial pressure constant at the value determind by the temperature.

From his work, it follows that the total pressure of a gas mixture could be divided into the constituent partial pressures of each component of the whole mixture. Thus -

$P_{ToT} = P_1 + P_2 + P_3 + \text{............} P_n$ (12)

These findings concur well with those of Charles and Gay-Lussac, in that when a gas is heated while in equilibrium with liquid water at a fixed total gas volume, the total pressure is the sum of the pressure of the variable mass of water in the gas, (determined solely by the vapour pressure of the water at that temperature), and the pressure of the fixed mass of non-water molecules.

Henry's Law

William Henry (1774-1836) was a close friend of Dalton and it appears that this friendship stimulated Henry into investigating further the solubility of gases in liquids. Henry studied medicine in Edinburgh, where his chemistry tutor was Joseph Black (1728-1799). Black discovered a new gas which he called "fixed air" (afterwards found to be CO_2) which he had found to be liberated by acids from mild alkalis and was given off by the lungs during respiration (16). He was aware that in 1772, Joseph Priestley (1733-1804) had reported to the Royal Society that heat or a vacuum would extract CO_2 from Pyrmont mineral water (20). Using Dalton's law of partial pressures, Henry attempted to quantify the relationships between solubility of gases in liquids.

In 1802, Henry reported that the quantity of CO_2 absorbed by water at 12.8 °C increased in direct proportion to its absolute temperature, which he raised to about 3 atm (21). He observed that when CO_2 was diluted by residual air in his apparatus, less CO_2 dissolved. This he concluded, was due to CO_2 dissolving in proportion to its partial pressure. Furthermore, he showed that the solubility of CO_2 decreased by about 1/14 for each 5.6 °C increase in temperature. Continuing his work further, he found that other gases behaved in a similar manner but had different solubility coefficients. The solubility coefficient of a particular gas is the volume of gas in ml that dissolves in each 1ml of liquid at a given temperature.

Henry's law therefore states that -

> "at a constant temperature, any gas physically dissolves in a liquid in proportion to its partial pressure, although the solubility coefficient decreases as temperature increases and differs from one gas to another".

This law only applies to physical solution and ignores any gas chemically combined (O_2 with Hb). Furthermore, it only holds for sparingly soluble gases at low pressure.

Graham's Law

Thomas Graham (1805-1869) first published on gaseous diffusion in 1829 (22). He had been drawn to the problem by an observation of Johann Wolfgang Doebereiner (1780-1849) that H_2 leaked out of a glass jar with a small crack, but other gases did not (23). This led him to study gas diffusion theory through porous materials such as unglazed Wedgewood, plaster of Paris and compressed graphite in the form of a porous disc (24). He found that bulk flow of gas through the disc was directly proportional to the difference in the total pressure of the gases in the two sides and inversely related to the porosity (the ratio of the volume of void space to the total volume). No distinction was made between the components of the mixture of gases.

When Graham placed two different gases (H_2 and air) inside a glass tube (D) inverted over mercury (figure 8) he found that each gas diffused through at its own rate, the rate being inversely proportional to the square root of its density. Hydrogen, having the lowest density diffused fastest.

Thus Graham's law states -

> "the rate of diffusion of a gas is inversely proportional to the square root of its density"

Applying this law today, we know that any temperature the mean kinetic energy ($mc^2/2$) for molecules of different gases of molecular mass m is the same. Thus:

$mc^2/2 = 3kT/2$ (13)

where k - the Boltzmann constant, is equal to R/L, L being the

Avogadro constant (the number of molecules in a mole of any substance).

If the subscripts A and H are used to denote air and H_2, then

$$m_A c^2_A/2 = m_H c^2_H/2 \tag{14}$$

or

$$c^2_A/c^2_H = m_H/2 \tag{15}$$

At any given temperature and pressure, the density of a gas p is proportional to its mass m, since equal volumes contain equal numbers of molecules. Therefore

$$m_H/m_A = p_H/p_A \tag{16}$$

Combining equation 16 with equation 15

$$c^2_A/c^2_H = p_H/p_A \tag{17}$$

and

$$\surd c^2_A/\surd c^2_H = \surd p_H \surd p_A \tag{18}$$

Equation 18 shows that the average molecular velocities are inversely proportional to the square roots of the densities of the gases. This explains why the rates of diffusion - which depend on molecular speeds - are also inversely proportional to the square root of the densities.

Further work by Graham showed this applied to gases without any porous barrier - free diffusion (25) and to the diffusion of solutes in a liquid (26)

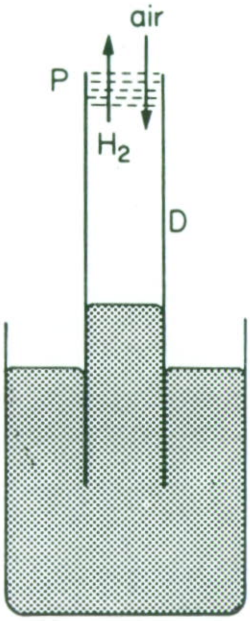

Figure 8. Graham's apparatus for diffusion. D is a glass tube, closed with a plug P of plaster of Paris. it is first filled with mercury, and inverted over mercury in a bowl. Hydrogen is pased into it until the mercury levels are the same on either side - the hydrogen is at atmospheric pressure. The apparatus is then left and hudrogen will difuse through P and air will diffuse in. Since hydrogen diffuses faster than air, the level of mercury inside the tube will rise. (Reproduced with permission from Advanced Level Physics, M Nelkon & P Parker, Heinemann Educational Books, 1977).

Fick's Law

Adolf Fick (1829-1901) demonstrated that for the diffusion of molecules the same laws apply as for the conduction of heat described mathematically by Joseph Fourier (1768-1830) (27).

Fick's law of diffusion states that -

"the transfer of a solute by diffusion is directly proportional to the cross-sectional area available for diffusion and to the difference in concentration per unit distance perpendicular to that cross-section".

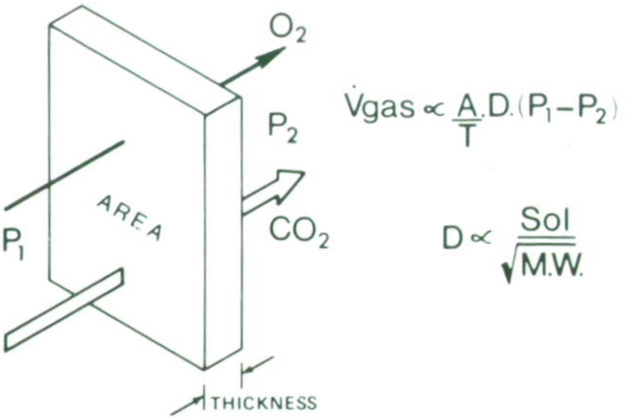

Figure 9. Diffusion of carbon dioxide and oxygen. The rate of diffusion (Vgas) is dependant on the cross-sectional area A and the thickness T and the partial pressure difference (P_1 - P_2) on the two sides of the membrane. The diffusion constant D is proportional to the solubility of the gas and is inversely proportional to the square root of its molecular weight. (Reproduced with permission from Respiratory Physiology - the essentials, 2nd Ed, JB West, Blackwell Scientific Publications, Oxford, 1983).

This is summarized in figure 9. From Henry's law, a very soluble gas such as CO_2 at a given partial pressure difference provides a greater concentration difference to drive its diffusion than for a less soluble gas such as O_2. As a result of this CO_2 diffuses about 20 times faster than O_2 through tissue sheets.

Franz Serafin Exner (1849-1926) combined this principle with Graham's Law to demonstrate that the relative diffusion of two gases, x and y, through a liquid barrier is directly proportional to the ratio of their solubilities and inversely proportional to the ratio of the square roots of the molecular weights (28).

Thus

$$Vx/Vy = (P'x - Px\ (a_x)(\surd\ MWy)(P'y - Py)(a_y)(\surd MWx) \tag{19}$$

where V is the volume of gas diffusing through the barrier per unit time, P′ and P are the partial pressures of the gases on the two sides of the barrier, *a* is the solubility of the gases and MW is the molecular weight.

Deviations from Ideal Gas Laws

With the basis of the behaviour of gases understood, there was a need to determine how each gas responded under different conditions.

Amontons (12) had suggested the concept of a temperature of absolute zero where gases would not exert any pressure. Many workers preferred to avoid this, and expressed thermal effects in terms of the fractional increases in pressure or volume when a gas was heated from freezing point to boiling point of water. This is the temperature at which the vapour pressure of water equals barometric pressure, which varies with the weather and altitude. This leads to potential errors in reproducibility.

Gay-Lussac obtained a value of 0.375 for the fractional expansion of dry air for this 100°C interval or 0.00375/°C (13). The reciprocal of this figure is 226.7, which at the time was the accepted number for conversion of Celsius to Kelvin. Any temperature on the Celsius scale can be converted to the Kelvin simply by adding 273.16 to it. This agreed with that of Dalton and was later confirmed by Pierre Louis Dulong (1785-1838) and Alexis Therese Petit (1791-1820) (29,30).

Frederick Rudberg (1800-1839) challenged this value in 1837, which from his own work indicated a value of 0.003646/°C giving a conversion factor of 274.3K (31,32). The reason for the difference between these and previous findings was that Rudberg measured the increase in pressure at almost constant volume (identical to Boyle's law) whilst Gay-Lussac had measured the increase in volume at a constant pressure. The differences observed are simply due to the different experimental conditions used.

Subsequently, Gustav Magnus (1802-1870) and Victor Regnault (1810-1878) began independently to investigate Rudberg's data further. In his studies Magnus (33,34) copied Rudburg in his experimental design by measuring pressure increase at constant volume and obtained a coefficient of expansion of 0.00366508 for air and a value of 0.00365659 for H_2. His value for CO_2 was somewhat different at 0.00369087, which he regarded as failure of CO_2 to obey Boyle's law. These figures give factors of 272.9, 273.5 and 270.9 for air, H_2 and CO_2 respectively.

Regnault initially obtained value of 0.003665 for air and 0.0036896 for CO_2 which agree with those of Magnus. Thus, there seemed to be a distinct difference between CO_2 and air. This led Regnault to undertake a major investigation of the thermal properties of gases which was financially aided by massive support from the French government. For almost 30 years, Regnault worked on the subject, producing 3 monumental publications which provide the most precise and extensive tables of experimental values available for many years. However, Regnault left the theoretical interpretation of his work to others.

With further refinements in technology and accuracy of techniques, the precise value for air is now accepted as 0.003660858, giving a value of 273.16. The measurement of absolute zero is based on a theoretical point. A volume of gas increases with temperature at a constant rate (Charles's law). However, all gases liquify at low temperatures (O_2 liquifies at −183 °C) and so the relationship of volume to temperature cannot be extended below this point. Nonetheless, a graph of the relationship of temperature and volume produces an essentially straight line, which, if projected to lower temperatures would cross the temperature axis at −273.16 °C. All gases produce the same result. This implies that if a gas could be cooled to −273.16 °C it would have zero volume and at even lower temperatures a negative volume! This is not possible, and therefore indicates that the lowest possible temperature is −273.16 °C. This appears to be confirmed by a number of recent experiments. On the Kelvin scale, −273.16 is referred to as "absolute zero".

Temperature Scales

With the adoption of the metric system, the comparison of data between different laboratories was very difficult. This was because there was no clear definition of the inch and hence the mm. It was accepted that the freezing point and boiling point of water were inadequate to define a temperature scale (37). Magnus used the boiling point of water at 760 mmHg as his standard whereas Rudberg used 28 Paris inches (757.96 mmHg). Before adoption of the metric system, the inch was defined in mm as 27.07 (Paris), 25.4 (British Imperial), 30 (Seden), 24-30 (Germany, depending which area one was in!)

The first reproducible liquid in gas thermometers calibrated using the freezing and boiling point of water were made with alcohol by Ole Christensen Romer (1664-1702) and were divided into equal subdivisions. Daniel Gabriel Fahrenheit (1686-1736), in conjunction with Romer developed the scale still used today, which is divided into 180° F. Rene-Antoine Ferchault de Reaumur (1683-1757) devised a scale commonly used in France which was divided into 80 R. Andreas Celsius (1701-1744) chose 100 divisions. Oddly, Celsius originally put the freezing point of water as 100 °C and his boiling point as 0 °C. Arl von Linne (1707-1778) was responsible for interchanging the values. The relationship between these scales is shown in figure 10. A fourth scale used in engineering measurements in the USA is that of Rankine (1820-1872) which is regarded as the absolute Fahrenheit scale. Zero degrees is equivalent to −460° F (−273 °C or 0 K) and 672 is equivalent to 212° F (100 °C or 373 K).

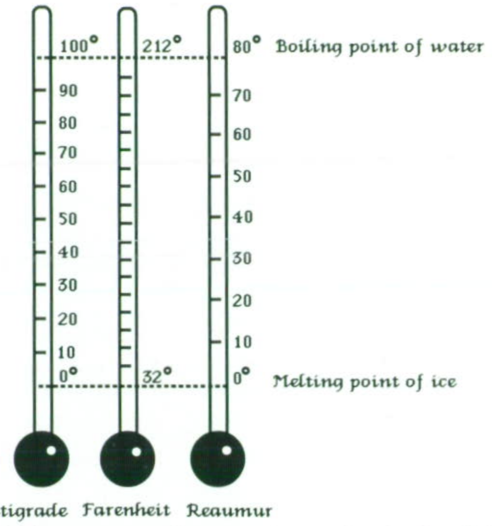

Figure 10. Thermometer scales comparing centigrade, Farenheit and Reaumur.

Dividing the temperature scale into equal divisions caused many problems, not least when one considers that mercury, alcohol and gases all expand alinearly when compared to each other. When this became clear from Regnault's work, William Thomson (1824-1907 - later to become Lord Kelvin) was already formulating the principles of thermodynamics (38) after being stimulated by Carnot's ideas about ideal heat energies (15). In 1848, he proposed an absolute thermodynamic temperature scale based on equal amounts per degree that would be independant of the expansion of any particular substance (39), developing it further with James Prescott Joule (1818-1889) and using Regnault's data. This is the reason why absolute temperature is expressed in degrees Kelvin today.

Van der Waal's Equation

Johannes Diderick van der Waals (1837-1923) attempted to refine the development of thermodynamic theory (40). Dalton's idea of individual gas particles each acting as if no other particle were present seemed incorrect to van der Waals. He later presented data (41) which linked the pressure (P), absolute temperature (T) and volume (V) of any gas by the equation -

$$nRT = (P + n^2a/V^2a)(v - nb) \qquad (15)$$

where a relates to the attraction force between molecules, b relates to their volume (both a and b vary with temperature), n is the number of moles of gas and R is the universal gas constant that links the various units used for the other variables and has a value of 8.3143 J/K/mol and T is in degrees Kelvin.

In pulmonary gas exchange a and b are usually assumed to be zero and therefore the relationship becomes -

$$PV = nRT \qquad (16)$$

This equation implies that at 273 K and 101.3 kPa, one mole of gas will occupy 22.4 litres. Although this is true for most gases that we breath, for CO_2 and N_2O the value is 22.26 litres (42). Van der Waals refinements to the ideal gas equation are important primarily when gases are under high pressures or at high densities.

Conclusion

The laws of physics and chemistry relevant to gas exchange have had a long and sometimes difficult gestation period to the present day. We owe a great deal to those who, in their various ways pioneered the work leading to the laws we now accept and use daily (albeit subconsciously!) in practical respiratory physiology. Without these laws we would never have been able to understand the process of gas exchange, use a body plethysmograph or even to develop SI units!

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Society Membership

There are currently 221 members of the Association. Those listed in the figure are currently working in hospitals within the NHS. The remainder are made up of staff employed either in non-NHS hospitals (private or military) or for companies with an interest in respiratory physiology. There are several regions with a very low membership and the Association would like to improve this situation. I would therefore encourage your colleagues to join the ARTP.

The Association is actively involved in the development of education and training for physiological measurement technicians. Assessments are held each year in Respiratory Physiology and a new venture started last year is a series of one and two day short courses on various aspects of respiratory function and measurement.

ARTP publishes its own journal - BREATH, three times per year and also circulates lists of job vacancies throughout the year. Two scientific meetings are held each year where members may present papers on research interests, case reports or other items of technical interest.

If you or your colleagues would like to join the ARTP, further details may be obtained from:-

Mrs V Hurt
Membership Secretary
Cardiothoracic Measurement Department
Derbyshire Royal Infirmary
London Road
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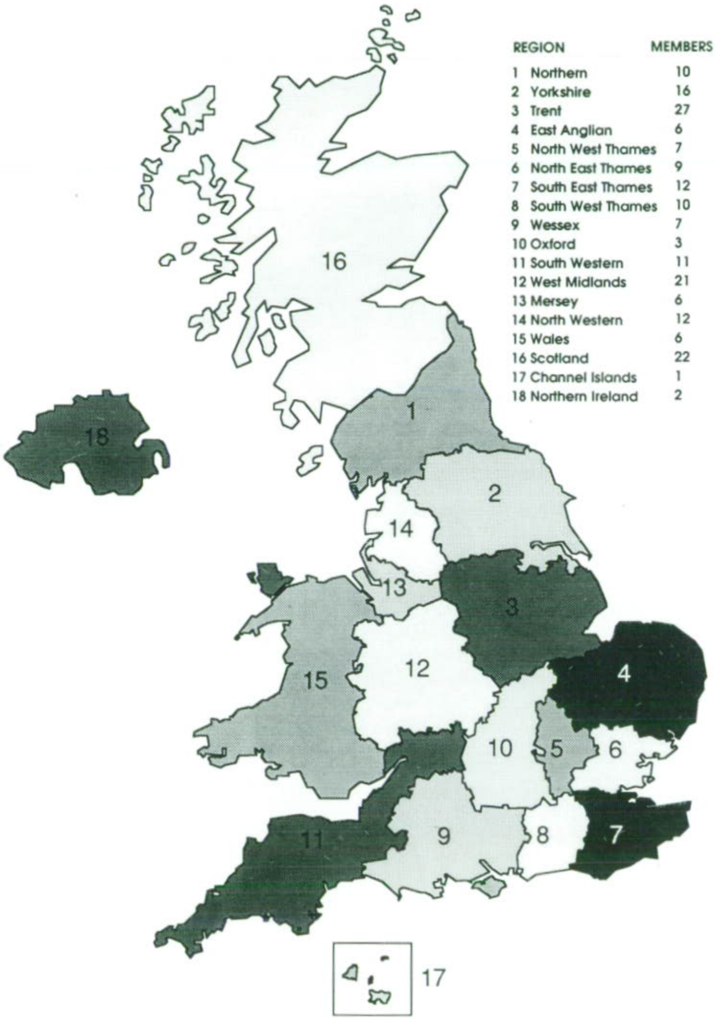

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Mr. Graham Wheeler has been appointed as the new Managing Director of Erich Jaeger UK Ltd as from 1st January, 1990.

Mr. Wheeler's previous position, was Business Group Marketing Manager for Philips Medical Systems UK and he has been involved in the Health Care Market for over seventeen years.

Association Meetings - 1990

This year marks the linking of ARTP Meetings with those of the British Thoracic Society who meet in July and December each year with their programme running from Wednesday morning to Friday afternoon. ARTP will be invited to attend the sessions on the Friday afternoon (at no charge) and will then continue with its own programme on Friday evening and Saturday. (The Friday afternoon session will include items of interest to ARTP members and in December ARTP will be organising a seminar on standardisation of techniques). The BTS, to encourage ARTP members to attend the major part of their meetings, have kindly made availabe 5 bursaries of £100 each. The bursaries are to go towards the cost of travel, registration fees and accommodation for the BTS meetings only.

The BTS summer meeting will be in Birmingham from 11 - 13 July 1990. Any ARTP member wishing to apply for a bursary to attend BTS should write to Dr. P. M. Tweeddale, Respiratory Function Laboratory, City Hospital, Greenbank Drive, Edinburgh EH10 5SB. ARTP will be meeting on the evening of 13 and all day on the 14 July 1990. Any person or group wishing to submit an abstract for the meeting should sent it to Dr. P. M. Tweeddale by 8th May 1990.

The Winter meeting will be held in London from 6th to 7th December, 1990. Details of this meeting will follow.

An opportunity will be given for members who do not receive funding from their departments to apply for assistance towards their travel expenses for the ARTP meeting.

We hope that the linking of the meetings with the BTS will be a successful venture and we encourage people to apply for the bursaries to attend the BTS meetings. We also look forward to seeing you at our summer meeting.

Short Courses

The Association will be holding two short courses as follows:-

30/31 May 1990 - Transfer Factor and Lung Volume
at Derby City Hospital

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Further details and registration from Vanessa Hurt, Membership Secretary

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Breath is the journal of the Association of Respiratory Technicians and Physiologists (ARTP) and is published three times a year. Members of the Association and non-members are invited to submit articles in the field of respiratory medicine, physiology or technology; articles relating to other disciplines are also welcome.

Two copies of an article should be submitted, as detailed below, to the Editor. Articles may be submitted to external referees for review prior to acceptance by the Editor. All articles are accepted on the understanding that they may undergo editorial revision.

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Material should be typed in double spacing on one side of the paper only and authors should keep one copy.

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These should follow the usual format of title page, a summary of 200 to 250 words, introduction, methods, results, discussion, acknowledgements, references, tables and legends to figures. The title page should give author(s), institution and address for correspondence. Each section should be clearly headed and started on a separate page.

Reviews

Reviews on topics of interest in the respiratory field and of books are welcome. Authors are requested to contact the Editor prior to submission of a review to ensure that the subject to be covered is not already in preparation. Reviews should generally follow the format of introduction, main body of text, references, tables and legends to figures.

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All letters should be addressed to the Editor.

Units and Symbols

The journal uses SI units only (except for blood pressure which should be in mm Hg). Abbreviations and symbols should be defined at first appearance. Acceptable units, symbols and abbreviations for lung function indices are given in Bull.Europ.Physiopath.Respir. Supp.5, 19, 52-61, 1983.

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Tables should each be typed on a separate page and numbered in order of appearance. Figures should be submitted as original art-work in black on a white background or as half-plate glossy prints, all marked on the reverse with the name of the first author and the figure number in order of appearance. Legends to figures and tables should enable them to be understood without reference to the text. Text in the legend should not be duplicated in the text of the article. In exceptional circumstances, colour figures may be accepted. Authors should contact the Editor prior to submission of colour prints.

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(2) Salahuddin SZ, Groopman JE, Markham PD et al (1984). HTLV-III in symptom-free seronegative persons. Lancet ii,1418-20.

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(1) Crofton J, Douglas A (1981). Respiratory diseases: 3rd Edn. Chap 15, 265-77. Blackwell Scientific Pubs. Oxford.

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New Printing Arrangements

After many years of valuable cooperation, we have ended our links with Stevens Brothers of Hackney in London, who have been responsible for printing 'Breath' since 1980. We owe very grateful thanks to Mr. Boughton, Mr. Moss and the staff at Stevens Brothers for all their help and advice and for the technical excellence of their production.

'Breath' will now be printed at the University of Bristol Printing Unit. The move to Bristol will much improve liaison between Adrian Kendrick and the printers and we will be better able to take advantage of modern printing technology.

We owe very grateful thanks to Leonette John, Cherry West, Catherine Fountain, Kay Yildiz and all others at the Lung Function Unit, the London Chest Hospital for all their help in the packaging and distribution of 'Breath' to the membership.