ASSOCIATION OF RESPIRATORY TECHNICIANS AND PHYSIOLOGISTS

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BREATH

CONTENTS

The migration of neutrophils into the lung.

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The inflammatory response was recognised by clinicians over two thousand years ago and the role of 'white cell' (or leucocyte) migration at the site of inflammation was described by Hunter as far back as 1794. We are now able to recognise several cell types which have an important role in this process, including the polymorphonuclear leucocyte (neutrophil). The neutrophil is one of the most potent weapons available in the human armamentarium in the fight against invading organisms. It has many functions some of which are outlined in Table 1. The neutrophil is 10-20 μm in diameter and has a multilobulated nucleus surrounded by cytoplasm laden with potent and destructive enzymes. Although the neutrophil is the most common leucocyte in circulating blood, only half of the total number are to be found in this compartment with the rest being loosely adherent to the vascular endothelium, particularly within the lungs. The circulating number of these cells rises rapidly within hours of the onset of inflammation and they are then concentrated at the inflamed site (1).

Once it has reached its destination the neutrophil interacts with other inflammatory cells in its quest to eliminate the inflammatory stimulus whether it be bacterial invasion, tissue injury (for example trauma or surgery) or as part of the perpetuation of an autoimmune disease (the body's defences being aimed at self with human proteins being recognised as antigenic or foreign). The response to a bacterial stimulus is most clearly demonstrated in patients with lobar pneumonia where there is a massive influx of neutrophils in response to the organism **Streptococcus pneumoniae** (Figures 1 and 2). This host defence process contributes to consolidation of the affected lung and containment of the invading organism. In the pre-antibiotic era such a rapid and effective inflammatory response to infection would have been life saving.

The rapid and specific movement of the neutrophil towards the site of inflammation and its role in pulmonary infection has received wide attention and now several stages are recognised (2):

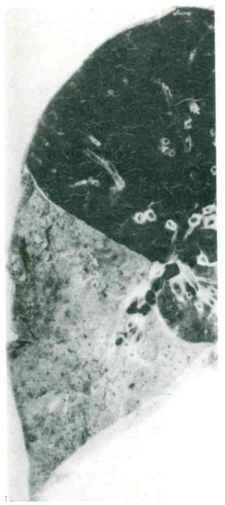


Figure 1. Post mortem specimen showing lobar consolidation in the lung of a patient who died from overwhelming pneumococcal pneumonia. The lower lobe is solid and airless as a result of the intense inflammatory response.

Aspects of neutrophil function

Chemotaxis	The directed movement of a neutrophil towards a stimulus, known as chemo-attractant or chemotaxin.
Chemokinesis	The random movement of a neutrophil following exposure to a chemo-attractant or chemotaxin.
Margination	The movement of a neutrophil from axial (or central) blood flow to the vessel wall.
Diapedesis	The squeezing of a neutrophil through the vessel wall into the interstitium.
Phagocytosis	The engulfing and ingestion of a bacterium by the neutrophil prior to bacterial killing.
Bacterial killing	The newly phagocytosed bacterium is exposed to proteinases and superoxide anions which result in its digestion and death.

Figure 2. H&E section (taken from Figure 1) illustrating the alveoli with the massive neutrophil influx that characterises pneumococcal pneumonia.

(a) Movement into the alveolus. In order for the neutrophil to be active at the site of inflammation it must move from the pulmonary capillary or venule through the alveolar basement membrane and into the alveolus. The first step in this process is dilatation of the local blood vessels which alters the flow characteristics of the blood and allows the neutrophil to move from the central blood stream (axial flow) to the periphery – a process known as margination or pavementing. The neutrophil then becomes more 'sticky' and adheres to the vascular membrane before passing through the endothelial cell junctions

into the interstitium of the lung, a process known as diapedesis (Figure 3). This movement of cells is associated with increased vascular permeability and the formation of an inflammatory plasma exudate.

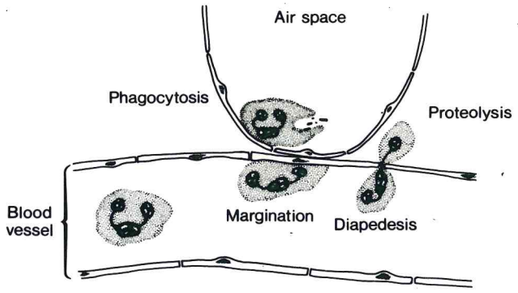


Figure 3. Diagrammatic representation of a neutrophil migrating through the endothelium of a blood vessel (by diapedesis) into the interstitium of the lung. This process is preceded by margination (see text) and followed by the ingestion of invading organisms (phagocytosis) and the release of enzymes which are capable of digesting protein (proteolysis).

(b) Movement from the interstitium towards the site of inflammation. During adhesion to the vascular endothelium and subsequent penetration into the interstitium, the neutrophil is exposed to a variety of stimuli which are able to influence its progress. These factors, termed chemotactic factors, chemo-attractants or chemotaxins, are able to increase its random movement (neutrophil chemokinesis) as well as determining the directional movement of the neutrophil (chemotaxis) (3). There are many such factors which may be produced by the invading bacterium, from the products of tissue injury, the complement cascade (4) or by monocytes, macrophages (leukotrienes and prostaglandins) and lymphocytes (lymphokines). Many of these mechanisms will act to recruit neutrophils during the inflammatory response and it is often difficult to dissect out the contribution of each individual factor.

(c) Changes within the neutrophil in response to chemo-attractants. A chemo-attractant acts on the neutrophil via a surface receptor. This in turn activates changes in the cyto-skeleton of the neutrophil allowing it to deform and so become orientated towards the stimulus (polarisation) (5). The cell then puts out an anterior projection or lamellipodium in the direction of movement and a posterior tail or uropod which points away from the chemo-attractant. The motility of these cells is dependent upon their infrastructure which consists of the contractile microfilaments, actin and myosin. These are powered by adenosine triphosphate (ATP), a product of the respiratory burst which follows exposure to a chemo-attractant.

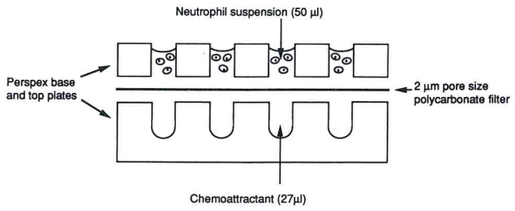
As the cell approaches the site of inflammation, so the chemo-attractant concentration rises which results in further activation of the neutrophil and so release of its stored products. These products include protein degrading (or proteolytic) enzymes (such as neutrophil elastase) and superoxide anions which probably have a role in the immobilisation and killing of bacteria.

At times however, such a response may be excessive and uncontrolled. In this situation there may be enormous numbers of neutrophils recruited to the lung and the enzymes that are released may themselves attack lung protein resulting in lung disease. Examples of conditions believed to be caused by this process include emphysema, adult respiratory distress syndrome, bleomycin induced pulmonary fibrosis and bronchiectasis. In bronchiectasis, the persistent inflammation (as demonstrated by the continuous production of purulent sputum) is associated with recruitment of large numbers of neutrophils to the lung. These, in addition to opposing the bacterial threat, release their proteolytic enzymes which are able to digest lung connective tissues and so may damage the lung further, thereby enhancing inflammation — the so called 'vicious circle' of events (6).

In such instances the patient may require drug therapy to attenuate neutrophil and other cellular function. The inhibition of neutrophil function, and in particular the suppression of cellular migration may be important in delaying the progression of these lung diseases. In order for this to be achieved there must be methods for the assessment of this modality of neutrophil function. Several techniques have been developed (7, 8), but there is a great deal of debate as to which most authentically represents the in vivo situation.

1. Modification of the Boyden Chamber (9, 10: Figure 4).

Neutrophils are isolated from peripheral blood or an inflammatory site and are placed in a suspension in the upper chamber. They are separated from the lower chamber which contains a chemo-attractant (such as the bacterial coat peptide, N-formyl-methionyl-leucyl-phenylalanine or FMLP) by a 2 μm polycarbonate membrane. Following incubation the membrane is stained and the number of cells which have moved through the membrane are counted (Figure 5). Such a method is rapid and relatively easy to perform and is useful when assessing soluble chemo-attractants. It is, however, difficult to differentiate chemokinesis (or random movement) from chemotaxis (gradient dependent directed movement) (8) and to relate cellular movement into a membrane to clinical practice.



Modification of the Boyden chamber (Falk et al, 1980)

Figure 4. Diagrammatic illustration of a microchemotaxis chamber. The cells (upper chamber) are separated from the chemoattractant (lower chamber) by a polycarbonate membrane. Following incubation the membrane is removed and stained so that the number of cells migrating to the lower surface may be counted.

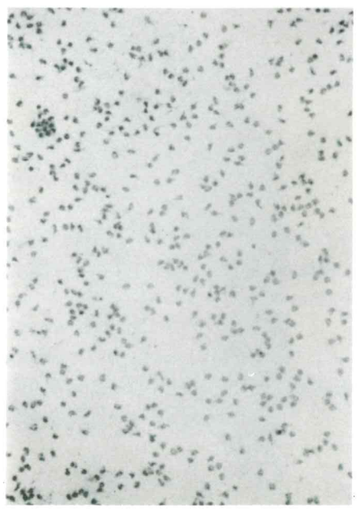


Figure 5. A stained membrane at ×400 magnification demonstrating neutrophils. These are then counted giving a measure of neutrophil chemotaxis.

2. Direct observation of a neutrophil migration (11).

The neutrophils are placed in a chamber with a chemotactic source (such as blastospores of Candida Albicans) and their movement towards the source is determined under the microscope with time-lapse cinephotomicrography. The technique is time consuming, difficult to perfect and awkward to quantify. It does however, allow for an accurate description of neutrophil migration.

3. Skin chambers to determine local leucocyte mobilisation (12).

A sterile plastic chamber is glued to a cleaned and abraded area on the forearm. The influx of neutrophils into the chamber can then be determined over a 24 hour period with various test solutions to detemine their chemotactic activity. The validity of this technique is uncertain as skin abrasion itself distorts the local vasculature and will affect neutrophil migration.

4. Radio-labelling of the subjects, neutrophils with indium-111 followed by infusion into the circulation (13).

The movement of neutrophils into the whole lung may be monitored by gamma camera imaging. This has been used to demonstrate an increased flux of neutrophils through the lungs of patients with severe bronchiectasis.

Clearly, only by following the radio-labelled neutrophils can one positively determine their movement within the lung, but this is cumbersome and of little practical value in determining the effect of various specific chemo-attractants on neutrophils from the peripheral blood or from bronchoalveolar lavage and then to assess their function in vitro.

A further indirect method of determining neutrophil response is to measure the release of neutrophil products such as neutrophil elastase, myeloperoxidase or lactoferrin. Sputum from patients with chronic airflow obstruction contains no demonstrable elastolytic activity; that is, it does not possess the capacity to digest the lung protein elastin. During infective exacerbations the sputum contains large numbers of inflammatory cells (particularly neutrophils) which release the enzyme elastase into the lungs. This overwhelms the protein inhibitors designed to inactivate the enzyme (such as α_1-1-antitrypsin) (14) and the sputum can be shown to be capable of digesting elastin (15). The quantity of neutrophil elastase is proportional to the neutrophil influx and also to the purulence of the sputum. Thus, by the observation of sputum purulence, as well as measurement of neutrophil products it is possible to assess neutrophil movement in response to an infecting organism (16).

The effects of therapeutic agents on neutrophil migration.

Studies performed in our laboratory have demonstrated that the non-steroidal anti-inflammatory drugs indomethacin and nabumetone reduce the ability of the neutrophil to migrate in response to an attracting stimulus after they have been taken continuously for 14 days (17). Furthermore, the potent anti-inflammatory drug dexamethasone is able to inhibit such a response within 2 hours of taking an oral dose (submitted for publication). Such drugs are not routinely used in the long term management of chronic lung disease but have a theoretical role in reducing the progression of these disorders.

A much more orthodox, but nevertheless still controversial therapeutic approach is to treat patients with severe bronchiectasis with long term antibiotics, either by the nebulised or oral route. It is believed that this serves to reduce bacterial load, reduce neutrophil migration into the lung and so reduce sputum purulence and increase patient wellbeing (18). This approach reduces the number of infective exacerbations of bronchiectasis and may in the long term delay the progression of lung damage.

Thus, it is clear that although the neutrophil is an important member of the 'host defence team', if its actions are excessive it may itself contribute to lung damage. It is also apparent that despite many years of study there is still no completely satisfactory method of assessing neutrophil movement in vitro or in vivo. Furthermore, many drugs may exert their effects by attenuating this modality of neutrophil function and in the future these may have a role in delaying the progression of destructive lung disease such as emphysema.

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The contribution of the pulmonary function laboratory in planning the treatment of congenital heart disease

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Introduction

Between five and eight per 1000 children will be born with some abnormality of the heart (1), ranging from the trivial which will correct itself with time, to major problems which are incompatible with survival. Some of the more common defects are shown diagramatically in Figures 1 and 2. At first sight, it seems unlikely that a lung function laboratory has any part to play in the treatment of these children. Indeed, the majority of such children require only echocardiography or a straightforward cardiac catheterisation in order to make the diagnosis and plan treatment. They then have corrective surgery, and subsequently, a normal life expectancy. A small minority present problems complicated by disease of the pulmonary circulation, and it is in these patients that the lung function unit can have a vital role in planning treatment. This paper begins with a brief account of the normal development of the lungs, which serves as a necessary background to the understanding of the effects of congenital heart disease. We then discuss work done at the Brompton using Fick cardiac output measurements, including the use of pulmonary vasodilators and the correlations between our measurements, lung damage, and outcome after surgery.

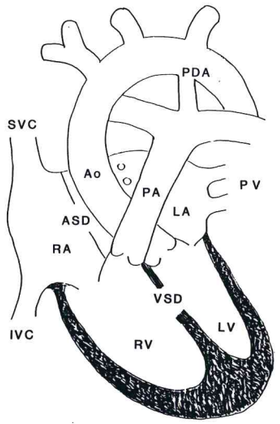

Figure 1. Some common congenital malformations. An atrial septal defect (ASD) is an abnormal connection between the right (RA) and left (LA) atria. A ventricular septal defect (VSD) is an abnormal connection between the right (RV) and left (LV) ventricles. A patent ductus arteriosus (PDA) joins the pulmonary artery (PA) to the aorta (Ao). Other abbreviations are: SVC, superior vena cava; IVC, inferior vena cava; PV, pulmonary veins.

Normal physiology

Before birth, the placenta is the organ of gas exchange. The two umbilical arteries run from the aorta to the placenta, which is drained by the single placental vein (Figure 3). Oxygenated blood (pO_2 30 – 35 mm Hg, or 4.0 – 4.5 kPa) is returned to the inferior vena cava, and thence to the right side of the heart (2). Very little of this blood enters the pulmonary circulation because the foetal lung only requires blood for nutrition, not for gas exchange (unlike the situation in postnatal life). Some blood flows from the right to the left atrium through the **oval foramen** (equivalent to an atrial septal defect). Some is ejected by the right ventricle into the main pulmonary artery. However, the resistance to flow offered by the pulmonary blood vessels (pulmonary vascular resistance) is high, and so most of the blood flows through a short, large

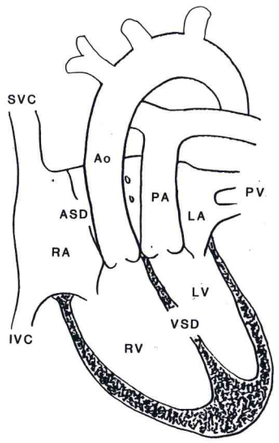

Figure 2. Transposition of the great arteries. The aorta comes off the right ventricle, the pulmonary artery from the left ventricle (compare with Figure 1). There is also an ASD and a VSD. (Abbreviations as Figure 1.)

vessel which joins the main pulmonary artery to the aorta, the **arterial duct** or **ductus arteriosus** The foetal pulmonary arteries and arterioles contain much more muscle than those of infants, related to the need to keep pulmonary vascular resistance high. Thus, compared to postnatal life, the foetal lungs have no function in gas exchange, a high vascular resistance and a low blood flow.

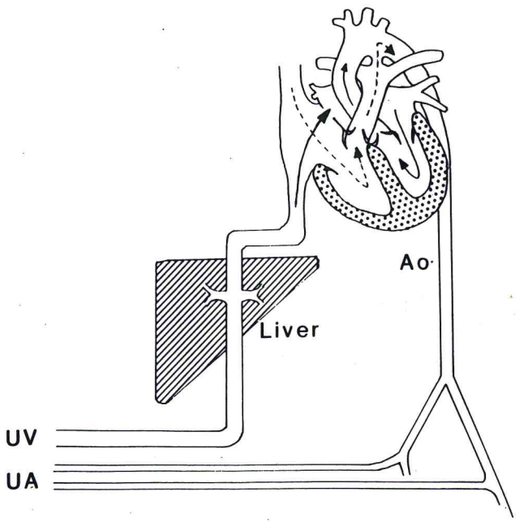

Figure 3. The foetal circulation (compare heart with Figure 1). Oxygenated blood returns to the heart from the placenta via the umbilical vein (UV). It is diverted through the oval foramen (equivalent to ASD) to the left atrium, left ventricle, aorta (Ao) and thence preferentially to the head and neck (solid line). Blood returning from the head and neck (dotted line) passes from right atrium, right ventricle and thence through the arterial duct (PDA) to the descending aorta. The circuit is completed by blood flowing from the aorta to the placenta via the umbilical arteries (UA).

At birth, the placenta is rapidly excluded from the circulation when the umbilical cord is tied and cut, and the lungs must immediately take over gas exchange if the child is to survive. During the passage of the baby down the birth canal, and especially during the first inflations of the lungs, the lung water content falls rapidly, predominantly due to drainage into the lung lymphatics (3). Pulmonary vascular resistance falls, and pulmonary blood flow rises. The oval foramen and the arterial duct cease to shunt blood right to left, although either may reopen in the days after birth. The control mechanisms for these dramatic changes are not known. One possible theory is that the fall in pulmonary vascular resistance is due to the release of prostaglandin D2 from perivascular mast cells (4). It is also possible that the mechanical effects of lung inflation on blood vessel calibre cause a fall in pulmonary vascular resistance (5).

During the early days of life, structural changes follow these functional events. The arterial duct seals off, and eventually is reduced to a thin solid cord of fibrous tissue. The oval foramen, which is more like a flap valve than an actual hole, seals off, although in up to a third of children, a probe at least can be pushed through it. The amount of muscle in the pulmonary arterial tree drops, and pulmonary vascular resistance remains low.

The lungs continue to increase in size for as long as the rest of the body is growing. However, early growth is by alveolar multiplication, whereas later, the increase in lung size is by increase in size of a fixed number of alveoli. The duration of the period of alveolar multiplication is controversial. It is variously stated to be complete by two to eight years of age (6,7). Many pathologists believe that the first two years of life are when the majority of alveolar multiplication takes place. The growing lung is therefore particularly vulnerable during this period.

Abnormal physiology

Heart defects may interfere with lung development. If there are abnormal connections between the right and left sides of the heart, the pulmonary circulation may be exposed to a high pressure or a high flow or both. The damaging consequences are the failure of the normal regression of vascular muscle at birth, and further increases in arterial muscle content. There is also proliferation of the intimal cells lining the arteries and arterioles, with eventual blockage of the smaller vessels. There is thus the potential for a self-perpetuating cycle (Figure 4). As the vessels become narrower, higher pressures are required to maintain pulmonary blood flow; and these higher pressures are a still more powerful stimulus to further narrowing of the vessels.

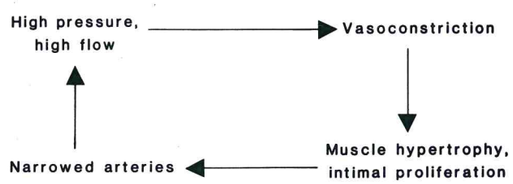

Figure 4. Self-perpetuating cycle leading to pulmonary vascular damage. Worsening vascular obstruction means higher driving pressures are needed, which in turn leads to worse damage. Eventually this becomes irreversible.

In the early stages, this cycle can successfully be interrupted by an operation on the heart having the effect of returning the pulmonary haemodynamics to normal. If the operation is successful, the pulmonary vascular abnormalities will partially or completely reverse. However, the damage to the pulmonary circulation may reach such a level that recovery is impossible, and the damage worsens whether or not an operation is performed.

In these cases, the defect in the heart is acting as a safety valve, decompressing the pulmonary circulation, and preventing pulmonary artery pressure rising too high. Closure of this safety valve at operation results in an impossible strain on the heart. In such cases, the child may well not survive surgery, or, if it does, life expectancy is even lower than if no operation had been performed.

The microscopy of damaged lung blood vessels

The assessment of pulmonary vascular damage, and hence prognosis, from lung tissue was first described on a systematic basis by Heath and Edwards in 1958, and their work forms the basis for most reports on lung biopsies (8). It is still the generally accepted "Gold Standard".

Heath and Edwards grades I and II are reversible, and are characterised by increased vascular muscle, and only minor thickening of the intimal lining. The conventional view is that this thickening of the muscle will get better if the cardiac lesion can successfully be corrected. In Grade III disease, the intimal lining becomes progressively thickened, initially by cellular proliferation, and later by fibrous tissue. Late Grade III, with fibrous intimal proliferation, is probably not reversible after operation. Grades IV or VI are now fairly rare, and are characterised by progressive proliferation and blockage of the small arterioles and intrapulmonary haemorrhage.

This classification has stood the test of time, but has its disadvantages. The main one is that it is qualitative, not quantitative, and pathologists often disagree on the severity of the disease. To try to overcome this, Rabinovitch and her colleagues described a new classification, in which the numbers of arteries and the thickness of the muscle wall is measured from the microscopic sections, expressed as mean and standard deviation, and compared to normal ranges (9). This classification shows less observer variation, but the assessments are very time-consuming.

Should the child have an operation?

Assessment of the pulmonary circulation requires knowledge not only of the level of the pulmonary vascular resistance, but also to what extent it can be reduced. If an elevation in pulmonary vascular resistance is found, this could be due either to fixed damage (which is what we want to measure) or to reversible vasoconstriction. The latter might be expected to improve after surgery. In order to measure only that part of the increased resistance which is due to fixed damage, we routinely give pulmonary vasodilators to reverse any constriction that may be present. Children with congenital heart disease are particularly prone to pulmonary vasoconstriction because of the increased amounts of muscle in the lung arterial system as described above. In many cases, it is clear from clinical examination and simple haemodynamic data that there is no significant damage to the pulmonary circulation. In doubtful cases, measurements of pulmonary vascular resistance are valuable. This requires the measurement of pulmonary blood flow and the pressure drop across the pulmonary circulation. The methods in routine use at the Brompton Hospital are described below.

Methods

1) Measurement of pulmonary vascular resistance In order to interpret pulmonary blood flow, it is necessary to know the pressure drop across the pulmonary circulation and thus whether flow is appropriate to the level of pressure. This allows the calculation of "pulmonary vascular resistance" (PVR), using the equation

PVR = (Mean PAP — Mean LAP)/Pulmonary blood flow

(where PAP and LAP are respectively the pulmonary and left atrial pressures, mm Hg). The normal value of PVR is less than 3 units (mm Hg litre^{-1} min per sq m body surface area), and does not vary significantly with age. Pulmonary vascular resistance is

an approximation, rather than a figure with a precise meaning. It assumes Poiseuille flow of a uniform fluid, which clearly never happens anywhere in the pulmonary circulation. It is, however, a clinically useful measurement.

2) The direct Fick principle The calculation of cardiac output relies simply on the law of conservation of matter, that is, matter can neither be created or destroyed. The matter or indicator substance generally used is oxygen. Considering the pulmonary capillary bed, in the steady state the amount of oxygen entering must equal the amount leaving, since oxygen cannot accumulate at any point.

Total O_2 input = O_2 input from airway + O_2 input from pulmonary artery blood

Airway O_2 input = Oxygen uptake by body (VO_2)

Blood O_2 input = Q (pulm blood flow) × PaOC

(where PaOC is pulmonary artery blood oxygen concentration in ml/L, and Q is pulmonary blood flow)

Oxygen leaving = Q × PvOC

(where PvOC is pulmonary vein blood oxygen concentration)
Therefore, $VO_2 + [Q \times PaOC] = Q \times PvOC$
rearranging this equation to give the familiar Fick equation,

$Q = VO_2/[PvOC - PaOC]$

Hence pulmonary blood flow can be calculated from measurements of oxygen uptake and the oxygen contents of pulmonary arterial and venous blood.

3) The measurement of oxygen consumption The method in routine use is the argon dilution technique (10). When the subject breathes air, the composition of inspired gas (including the percentage of Argon) is known. All the expired gases are collected and passed through a mixing box. At the entrance to the box a stream of 100% argon is injected at a known and constant flow rate. After mixing, the gases are sampled by the mass spectrometer, using a long, flexible probe. The greater the expiratory flow rate, the greater the dilution of the stream of argon. Knowing the expiratory flow rate and the partial pressures of the components of inspired and expired gases it is possible to calculate VO_2 and carbon dioxide production (VCO_2), and hence respiratory quotient (RQ, = VCO_2/VO_2). End-tidal pCO_2 is also measured to check that a respiratory steady state is present, and as a guide to alveolar gas tensions, which are sometimes used in the calculations. When the subject breathes 100% oxygen, provided a respiratory steady state exists, RQ is assumed to be unchanged, and VO_2 is calculated from the measured VCO_2 (=VCO_2/RQ).

These children are studied at the time of cardiac catheterisation, for which they need a general anaesthetic. Oxygen consumption must be measured directly, because prediction equations, which are usually extrapolations from older, normal children studied without anaesthesia, are often very inaccurate (10). Other methods of measuring cardiac output, such as thermodilution and dye dilution, are not valid if there is any shunting.

4) Measurement of blood oxygen content This can be measured directly, but the instruments tend to be too slow to use in studies in which a large number of samples are taken over a short time. We therefore calculate oxygen content using measured blood pO_2, pH and base excess, and using Kelman's subroutine (11).

The use of pulmonary vasodilators

Early studies on the reversibility of an elevated PVR used 100% oxygen; interestingly, O_2 is a pulmonary vasodilator even in those with no alveolar hypoxia. It increases aortic pO_2 and acts as a systemic vasoconstrictor. All other pulmonary vasodilators also dilate the systemic circulation, and this may lead to a fall in aortic pressure and venous return to the right heart, paradoxically lowering cardiac output. They may also worsen systemic oxygenation, by impairing ventilation-perfusion matching in the lung. This is important, because the effect may be a lower flow of more poorly oxygenated blood to the heart, and death may result. These adverse effects of pulmonary vasodilators underline the need to measure their effects with great care.

We obtained dose response curves for the effects of Prostacyclin (PGI_2) given by continuous intravenous infusion (12). When the patients breathed air, PGI_2 caused a dose-dependent fall in PVR. This resulted from an increase in pulmonary blood flow, with little change in pulmonary artery pressure; were only pressure to have been measured, PGI_2 would have been discarded as inactive. With the infants breathing air, PGI_2 (20 ng/kg/min) was equally as potent a pulmonary vasodilator as when they breathed 100% oxygen alone. When PGI_2 was added to 100% oxygen, there was a further dose-dependent fall in resistance. PGI_2 caused a dose dependent fall in mean aortic pressure on both air and 100% oxygen. We concluded from this study that an airway borne vasodilator (100% oxygen) in combination with a bloodborne vasodilator (PGI_2) is useful in the management of these children. We now routinely measure PVR pre-operatively in children with pulmonary hypertension on air alone and on 100% oxygen, alone and in combination with PGI_2 (5-20 ng/kg/min).

Relationship between vascular damage and PVR

The advantage of the physiological methods outlined above is that the results are obtained at the time of a necessary diagnostic procedure, without additional risk to the child. All histological methods have the drawback of requiring a general anaesthetic and a thoracotomy in order to perform a lung biopsy. This carries an additional risk, particularly in the critically ill child. We therefore compared the physiological methods with lung microscopy and eventual outcome (13). In a highly selected group of patients with suspected pulmonary vascular disease, we showed that a high PVR (>6.5 units) despite pulmonary vasodilators predicted a poor outcome. In some patients this was because of severe irreversible pulmonary vascular disease (Heath and Edwards late Grade III or worse). In others, there was very greatly increased pulmonary arterial muscle which might have improved with successful surgery (Heath and Edwards Grade I or II). However, these patients had a stormy peri-operative course, and most died without ever leaving intensive care. Patients with a low PVR and Heath and Edwards Grade I or II generally did well.

Summary and conclusions

The pulmonary function laboratory clearly has a role in the measurement of disability and the assessment of the results of operation, for example using exercise tests. The effects of heart disease on lung growth, and hence lung size, can be assessed by standard lung function tests. This article has discussed a more specialised role of the pulmonary function laboratory in deciding whether pulmonary vascular disease precludes a successful heart operation, and optimising the use of pulmonary vasodilators. This role will only be needed in large centres which specialise in heart disease in children, but in such centres, the laboratory will allow rational planning of treatment of pulmonary circulatory disorders, rather than the use of guesswork.

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BTS/ARTP Meeting – December 6-8th 1990

Following the first joint meeting in July 1990, the winter meeting of both societies will take place at Kensington Town Hall, London.

On Friday 7th December, a joint symposium entitled:

"The Lung Function Laboratory in the 1990's"

will take place, to which technicians and their clinicians are invited to attend. Speakers will include GJ Gibson (Newcastle), Ph Quanjer (Leiden), SL Hill (Birmingham) and AH Kendrick (Bristol).

The ARTP meeting, including the AGM will take place on Friday evening and all day Saturday.

Guidelines for Contributors to 'Breath'

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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

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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.

Tables and Figures

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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Original Article
(1) Depledge MH, Barrett A (1981). Aseptic techniques for lung function testing. J Hosp Infec:2:369-72.
For more than 3 authors –
(2) Salahuddin SZ, Groopman JE, Markham PD et al (1984). HTLV-III in symptom-free seronegative persons. Lancet ii,1418-20.

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

Section in Edited Book
(1) Morgan PK (1983). Physical Gas Analysers. In: Measurement in Clinical Respiratory Physiology. Eds Laszlo G, Sudlow MF. Academic Press, 113-30.

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