CHAPTER 2 - SHORTNESS OF BREATH

INTRODUCTION

In this chapter, we look at the way we approach clinical problem-solving in patients whose major presentation is of DYSPNOEA or shortness of breath. We do this again in our four diagnostic categories, narrowing down hierarchically in each, especially in this case in relation to the Anatomical diagnosis of the organ system involved.
This chapter discusses respiratory causes of shortness of breath. You might think that localizing a respiratory origin to this symptom would be relatively easy, not only because shortness of breath is such a prominent symptom in respiratory disease, but also because of the association in the history of other features such as wheeze, cough, sputum, haemoptysis etc., and the accessibility of the chest (and sputum) to physical examination. In addition, because the lung's primary function is to ensure adequate gas exchange of 02 and CO2icross the alveolo-capillary membrane, any defect in the exchange of either of these gases should give classical clinical signs. However, there are several important principles in clinical respiratory physiology that must be discussed before we can apply our approach to clinical problem-solving to this system.

Gaseous Exchange in the Lung and Oxygen Delivery to the Tissues

First, what matters to the body is tissue oxygen delivery, and so the lung cannot be viewed as an isolated unit, but only in harness with the circulation. For example, no matter how well oxygen is delivered to the pulmonary capillaries and CO2 taken up into the alveoli from them across the alveolo-capillary membrane, if the cardiac output is low, or oxygen-carrying capacity of the blood (haemoglobin concentration) reduced, there will still be tissue hyoxia. And sometimes, even if there is respiratory disease limiting the degree of alveolo-capillary gaseous exchange, as well as the low cardiac output, very low tissue oxygen delivery may occur without being evident as central cyanosis either clinically or on blood gas analysis, because the increased pulmonary capillary transit time of blood (from reduced cardiac output) means that there is more time for gaseous exchange to occur in the alveoli. Then, the arterial pO2 and pCO2 may even be normal, but delivery of 02 to the tissues impaired. So we must assess respiratory system function together with the cardiovascular system, and peripheral tissue perfusion to determine the adequacy of tissue 02 delivery.

Hence a general point, viz: that we tend to teach and practice medicine in the specialist areas of different systems, but it is important to take an integrated view of, and get a good grounding in, general physiology and medicine, before pursuing any narrower specialist path. Indeed, some of the best contributions good specialist physicians make to patient-diagnosis is the recognition that the primary or basic abnormality they see lies outside their own particular field of interest or expertise.

Some problems.

1. The first is to define what we mean by shortness of breath. You might think, from your own experience on exercise, that shortness of breath would be a symptom directly related to the degree of lung ventilation (litres per minute respired), but this turns out not to be so, for a number of reasons. First, shortness of breath is a subjective sensation, and some patients have an awareness threshold much greater than others, just as with pain. Second, patients with acute onset shortness of breath usually notice much more distress than those where the onset has been gradual. At the other end of the scale, patients with anxiety states frequently complain of "shortness of breath", without having any abnormality in the lungs or heart at all. This category is important to dissect off, because it is common, and is generally relatively simple, because on close questioning you can usually elicit its special features, viz. not so much a "puffing and panting" as "a feeling of not being able to get enough air into my lungs", often associated with deep sighing respirations which you can readily observe during history taking. In addition, there are usually other features of anxiety, restlessness and/or helplessness; and, of course, there are no objective signs of organic cardio-pulmonary disease. But be careful even here, because many patients with real organic pulmonary, cardiac, and other disease can be understandably anxious about their disease. Also, patients with chronic anxiety states may develop organic disease the same as anyone else.

2. Difficulty in defining dyspnoea. If we take patients with definite (say lung) disease with similar degrees of functional impairment (i.e. similar arterial pO2 and pCO2) their complaints of shortness of breath are often vastly different. When one analyses such patients, it is usually those with laboured respiration due to airways obstruction and/or reduced lung compliance (increased "stiffness") who complain most of shortness of breath. This has led to the concept that it is the work of respiration which best defines dyspnoea or perhaps more precisely, the degree of imbalance or inappropriateness between the body's demand for respiratory ventilation and the *forces* required to meet this demand. This is probably the most important element in the subjective feeling of dyspnoea in most cases (though precise mechanisms remain obscure). Going a step further, I take the view that normal respiration is an automatic unconscious process, so it is likely that the conscious feeling of shortness of breath will only come about when the drive to respiration has spread to reach the conscious level, i.e. when there is extensive (conscious) recruitment of accessory muscles of respiration such as the trapezius, sternomastoids etc. to fix the shoulder girdle and give a greater ("pump handle") mechanical advantage to the upper chest - a level which has to be driven consciously. This may also help explain why some patients can have obviously excessive lung ventilation (litres per minute) to the observer (as in metabolic acidosis, severe anaemia etc.) but be without any subjective feeling of shortness of breath at all, because their lungs, being normal, do not require a great increase in respiratory effort to maintain high ventilatory rates, i.e. in my terms respiration is still an unconscious process. Despite all this, it must be said that we are still ignorant about many aspects of dyspnoea. In some cases, there may be a superimposed input from (vagal) receptors in the pulmonary arteries as in pulmonary embolism.

FIRST LEVEL ANATOMICAL DIAGNOSIS IN CASES OF DYSPNOEA

Which organ SYSTEM is involved?
From the foregoing, we can, by our hierarchic approach to questioning in the history, separate off metabolic (e.g. metabolic acidosis, anaemia) and psychogenic causes of shortness of breath, which leaves us, broadly speaking, with the two organic causes, namely pulmonary and cardiovascular.

Cardiovascular causes can be further dissected off in our hierarchic approach because of the usually associated presence of orthopnoea (shortness of breath on lying flat). This is characteristic of impairment of left heart function because in that situation the pulmonary venous pressure rises significantly with the adoption of the recumbent posture due to transfer of blood from the legs to the pulmonary circuit, so increasing pulmonary venous pressure even more than the already elevated level. Initially this merely causes congestion of the alveolar capillaries, bu this alone may be sufficient to cause stiffening within their walls, and hence a reduced pulmonary compliance, so making the work of respiration difficult. Many patients seem to sense this as 'discomfort' even before they notice 'shortness of breath', and compensate for it by sleeping on an increasing number of pillows at night. Others seem to have less appreciation because they get off to sleep well enough, but as the night goes by, increasing capillary pressure and dilatation from pulmonary venous "back-pressure" leads to transudation of fluid across the capillary walls through the alveolar interstitium. To a certain extent, this fluid can be coped with by increased lymphatic lung drainage, but this has a limit, and fluid eventually overflows into the alveoli. At that stage, even the soundest sleeper awakes with shortness of breath (P.N.D.), and in severe cases they cough up frothy pink-stained fluid (i.e. red blood cells as well as fluid transuded through the capillary walls). This shortness of breath is classically relieved by adoption of the upright posture, usually within 20 minutes. If examined during such an attack, the characteristic signs are extreme dyspnoea, frothy pink sputum, central cyanosis, and fine late inspiratory crackles or crepitations, particularly marked at the lung bases posteriorly. All this emphasizes the importance of clinical physiology and functional diagnosis can be to our Anatomical diagnosis.

Several notes of caution about diagnosing cardiac dyspnoea (left heart impairment/failure). First, early on, patients may not complain of any orthopnoea, and you will be dependent on finding appropriate cardiac signs to localize anatomy correctly. Second, even being woken short of breath at night is not sufficient for a diagnosis of a cardiac cause, because bronchial asthma may also occur at night - indeed, early morning (about 5.00 am) "dipping" wheeze is a common early feature of poorly controlled bronchial asthma. Third, as well as crepitations (alveolar fluid), patients with left heart failure can have the increased "back-pressure" transmitted to the bronchioles, so producing oedema of bronchiolar walls, and narrowing of the airways resistance pathways, with consequent wheeze.

The greatest difficulty is in deciding whether a patient has chronic obstructive airways disease (C.O.A.D.) with an acute exacerbation precipitated by acute bronchitis and bronchiolitis (lung wheezes and crepitations) followed by secondary hypoxia, pulmonary hypertension and (right) heart failure or on the other hand, whether he has primary (left) heart disease with secondary pulmonary involvement causing alveolar and bronchiolar oedema (crepitations, wheezes), consequent

pulmonary hypertension and secondary right heart failure. Yet this distinction is extremely important therapeutically.

We should now inquire further not only into the type of shortness of breath (whether inspiration or expiration is more difficult, presence of wheeze, etc.) but also about other respiratory system symptoms and their time-intensity relationships, to give us a more complete anatomico-pathological diagnosis. Classic symptoms are cough, sputum, haemoptysis, chest pain, weight loss, & fever. The last two are, as usual, helpful in our clinical *pathological* diagnosis (e.g. acute inflammation), but in the respiratory system we can also get evidence of local inflammation/infection by examination of the sputum.Yellow or greenish-yellow sputum suggests an inflammatory cause (neutrophils) or asthma (eosinophils), Haemoptysis can contribute to both the anatomical and pathological diagnoses; in the latter respect it suggests ulceration, vascular rupture or infarction. If recent onset acute pulmonary infarction, trauma, or vascular rupture are also possibilities, but if chronic, then ulceration (e.g. from neoplasia) is more likely (is there associated weight loss?). Anatomically, blood uniformly mixed with sputum (as in pulmonary infarction, acute pulmonary oedema, haemorrhagic alveolar disease) suggests peripheral lung involvement, whereas blood streaking of sputum suggests involvement much higher up in the bronchial tree.

Cough give us more information about anatomy than pathology. In particular, a dry cough suggests involvement of the upper airways, especially of the trachea and bronchi, because this is where nerve endings for cough occur. Thus, dry cough might suggest infiltrating neoplasm, or mediastinal pressure on the trachea from lymph nodes, etc. or bronchitis, depending on other clinical features. Some medications also cause dry cough, particularly the ACEI drugs used in hypertension. Of course, when a cough is productive of sputum it is difficult to separate cause and effect, because it may be due to secretions being brought up to the trachea from further down the lung through normal broncho-cilial action.

Pain does not arise from the lung per se, and usually points to an involvement of the parietal pleura, or chest wall. As with any other symptom, its nature, radiation, aggravating and relieving factors, are helpful in anatomical diagnosis, and this is particularly true of pleural involvement, which gives a sharp localized pain aggravated by inspiration and coughing, and eased by splinting the area e.g. with the hands. An inflammed trachea can give rise to certain soreness behind the upper sternum, as we all know.

Respiratory system examination usually improves our anatomico-pathological diagnosis further. First, a knowledge of the surface markings of the various lung lobes, plus the ability to detect by inspection, palpation, percussion and auscultation, the various signs of consolidation, collapse (with or without bronchial obstruction), pleural effusion, pneumothorax, and emphysema, should allow you to make an accurate anatomical diagnosis. Second, general examination (temperature chart, weight loss), chest signs and inspection of sputum, where yellow or yellow/green colour usually signifies inflammation (microscopy, Gram stain, culture to confirm).

Overlap between the Pathology and Anatomy categories can contribute to diagnosis in each. This is particularly true with very acute onset conditions which give the clue that the clinical pathology is one of acute obstruction or rupture of hollow tubes. These can be vascular structures (pulmonary congestion, pulmonary embolism), or the airways themselves in obstrution or rupture to produce dramatic clinical events (e.g. acute bronchial asthma and spontaneous pneumothorax respectively).

Functional diagnosis can also contribute to our anatomical diagnosis, so we now consider this.

FUNCTIONAL DIAGNOSIS

In many cases, the functional diagnosis is simple, perhaps because the lung has a relatively simple function in terms of gaseous exchange. Thus, pulmonary dysfunction may cause alterations of arterial pO2 and pCO2, and these alterations should be recognizable clinically.

Hypoxia (low arterial pO2) should be recognisable as (central) cyanosis, and usually is, but a few comments. First, distinguish peripheral from central cyanosis, and in this respect do not think of the word "peripheral" so much in the anatomical sense as the physiological one. Thus, a patient with cold hands may have peripheral cyanosis both in the anatomical and physiological sense, but where the patients hands are warm and well perfused, you can use them to gauge the degree of central cyanosis (in the physiological sense). This is important, because if both your hands and the patient's are warm, you can compare the colour of the two. This gives a much more sensitive index of central cyanosis than, say, just looking at the tongue. Such factors have helped us to detect cyanosis at a much earlier level than was once thought. Thus, it used to be said that it required 5g/dl of unsaturated haemoglobin to detect cyanosis clinically, but from our knowledge of the oxygen-dissociation curve, that would mean that in ordinary circumstances we would not detect cyanosis until the patient had extreme hypoxia.

This brings us to the important figures to remember in relation to the haemoglobin oxygen dissociation curve, namely that haemoglobin is normally 95-98% saturated when breathing room air (alveolar p02 = 90-115 mm Hg); but because of the flat part of its upper oxygen dissociation curve, it remains fairly well saturated at surprisingly low levels of arterial pO2. Importantly, it is approx.

* 90% saturated at an arterial pO2 of approx. 60 mm Hg;

* 75% saturated at arterial pO2 of 40 mm Hg; and only drops to

* 50% saturation at approx arterial pO2 of 25 mm Hg.

Of course, these values are approximate, because the oxygen dissociation curve is influenced by acidosis, PCO2, 2-3 DPG etc. But, they are exceedingly important rules of thumb for working out clinical blood gas problems. To illustrate, a patient with a haemoglobin of 16 g/dl and an arterial pO2 40 mm Hg would have 75% (12 g/dl) of haemoglobin saturated, and 25% (4 g/dl) unsaturated, and if the old rule above were true that we needed at least 5 g/dl unsaturated haemoglobin to detect cyanosis clinically, then even this patient would not be cyanosed! We now believe however, that we can detect 1.5 g/dl unsaturated haemoglobin, and at normal haemoglobin levels this occurs at 90% saturation (10% of 15 g/dl haemoglobin = 1.5 g/dl); and, as we know, this normally occurs with an arterial pO2 of approximately 60 mm Hg. Note that the patient's haemoglobin level is important in this equation. Thus, patients with an increased haemoglobin (polycythaemia) will become much more readily cyanosed than normal at a given level of arterial pO2, while in anaemic subjects cyanosis may not become apparent even with very low levels of arterial pO2, because it is the absolute amount of unsaturated haemoglobin per unit volume of blood which determines the degree of central cyanosis, not the relative one.

Some important normal values to remember.

1. Arterial blood haemoglobin is almost fully saturated (98%) and, with a haemoglobin level of 15g/ 100 ml, contains 20 ml. O2 per 100 ml. blood.

2. Venous blood is normally 75% saturated (PO2 = 40) in most beds. From 1. above, this = 15 ml. 02 per 100 ml. in venous blood (much less in coronary sinus). Thus. 5 ml of O2 extracted during each 100 ml. of blood passaged through the capillary bed.

3. Blood volume is approximately 5 litres.

4. Cardiac output is approximately 5 litres per minute.

5. Normal ventilation is approximately 5 litres per minute.

6. Therefore, from 1-5 above, 250 ml. O2 are normally taken up by the blood from the lungs every minute at rest.

Clinical signs of blood gas changes

Apart from hypoxaemia (low arterial pO2), we should be able to recognize the clinical signs associated with altered arterial pCO2. Thus, hypocapnia (low arterial pCO2) leads to characteristic and usually quite recognizable signs, namely systemic arteriolar constriction giving rise to light-headedness (cerebral vasoconstriction reducing brain blood flow) and pallor of the skin. In addition, reduced arterial pCO2 causes alkalosis, which diminishes the concentration of plasma ionised calcium, important in nervous transmission. Hence the symptoms of tingling or parasthesiae,

particularly the hands, feet and around the mouth, as well as the characteristic carpo-pedal spasm in extreme cases. Anxiety-invoked hyperventilation blowing off excess CO2 is a typical example.

Carbon dioxide retention, on the other hand, leads to hypercapnia (increased arterial pCO2), and this has quite different and readily distinguishable signs. The main affect of an increased arterial pCO2 is peripheral (systemic) arteriolar dilatation, giving rise to classical signs. The first are due to capillary dilatation and include warm hands and, because of the increased capillary pressure, sometimes dependent oedema as well. In severe cases, even the brain becomes oedematous with clouding of consciousness, and even papilloedema. The circulation has a tight regulation, particularly of systemic blood pressure, so when systemic arterioles dilate, and blood pressure tends to fall as a result, there is a compensatory increase in cardiac output, and this gives rise to tachycardia, large volume pulse, and contributes to the increased warmth of the hands.

Thus, where there are clinical signs of hypoxaemia, hypocapnia or hypercapnia, one would imagine that it would be a relatively simple matter to make a diagnosis of the type of pulmonary dysfunction involved, and hence strengthen the anatomical diagnosis. For example, obstruction of the airways should, one would think, result in hypoxaemia and CO2 retention, with all of the characteristic signs discussed above. And we certainly see this, say, with extrathoracic tracheal or laryngeal obstruction. Under these circumstances, hypoxia rapidly develops together with hypercapnia, and the latter provides a particularly strong drive to respiratory effort - to no avail in this situation. On the other side of the coin, non-obstructive more interstitial lung disease such as pulmonary fibrosis should, one would imagine, interfere not so much with gaseous movement into and out of the alveolus, but with the transfer of gases across the (thickened) alveolo-capillary membrane. And this, too, should be helpful in diagnosis, because CO2 is known to be more diffusible through the alveolo-capillary membrane than oxygen, and in these circumstances, we often do find the clinical signs of hypoxaemia without evidence of CO2 retention.

However, although this may all sound common sense, things are often much more difficult in the clinical setting. First, intra-thoracic obstructive airways disease is not nearly as straightforward as this in practice. Thus, although the predicted hypoxaemia occurs, CO2 retention is the exception rather than the rule! - at least in acute cases. Moreover, what we recognize as obstructive airways disease may be associated with an overall *increase* in ventilation (hyperventilation) in terms of litres/minute respired.

This brings us to our first paradox, namely how can we talk of obstructive airways disease when the overall minute rate of ventilation is increased? - particularly if there is continued hypoxaemia without CO2 retention, because in obstructive airways disease, alveolar hyperventilation sufficient to blow off CO2 should surely also normalize alveolar pO2 (remember that alveolo-capillary membrane itself is normal in this condition). We therefore have to dissect lung function a little further, looking firstly at the mechanics of respiration, and then at the concept of ventilation/perfusion matching and mismatching, before being in a position to use effectively our clinical signs of blood gas alteration in working out the Functional nature of the problem confronting us in individual patients.

The Mechanics of Respiration

(a) Acute Airways Obstruction

The normal resting position of the thorax is the dynamic result of the natural tendency of the lungs to collapse on the one hand (due to their elastic recoil) and the tendency of the rib cage to oppose this. This results in a negative intrapleural pressure during inspiration. Inspiration is an active process, but normally expiration is passive (lung elastic recoil). Second, there is a greater resistance to flow in the airways within the chest during expiration than during inspiration. This increased resistance to intra-thoracic airways flow during expiration comes about as follows: The alveoli around the terminal bronchioles (which lack cartilege) have a higher expiratory pressure than the terminal bronchioles themselves (otherwise there would be no flow of air out of the lung during expiration), and this increased pressure tends to collapse the terminal bronchioles during expiration. Now this may not particularly matter in normal people, where bronchioles still remain reasonably patent even at end-expiration, but when there is airways narrowing (either acute or chronic), it may become a highly significant factor, because the consequent greater airways resistance to flow during expiration will lead to the expulsion of a lesser quantity of air than inspired, resulting in gradual hyper-inflation of the alveoli (i.e. an increased residual lung volume). Fortunately, this is a self-limiting process (at least in the acute phase), because the stretched alveoli develop an increased elastic recoil, so improving the force of expiration and, with it, an increase in the volume of air expired. You might think that expiratory flow could also be increased by making the expiratory phase of the respiratory cycle more forceful than the passive process it normally is, and indeed this often occurs. However, in practice, its value is limited because forced expiration not only increases intra-thoracic pressure but the pressure within the alveoli, and hence the surrounding pressure tending to collapse the small bronchioles during expiration. So, far from improving the problem, forced expiration may actually increase the resistance to flow during expiration. It also tends to produce alvoelar "air-trapping" in the segments of lung involved. But to overcome this, some patients (particularly those with COPD) learn to overcome this to some degree by putting a "backing-pressure" on the alveoli and terminal bronchioles so as to hold them open during expiration. This they do by pursing their lips during each (prolonged) expiration. The same effect can be achieved during artificial ventilation by placing a resistance in the expiratory circuit (positive end expiratory pressure or PEEP), although there is a limit to the benefit of this in terms of systemic tissue oxygenation, because too much PEEP will limit venous return and therefore cardiac output!

These aspects of ventilatory mechanics are common to both acute and chronic airways obstruction. However, there are aspects of each which we should consider separately. In relation to acute airways obstruction ("bronchial asthma") there are several points. First, in the typical attack, it is the bronchioles that are narrowed. This provides an increased resistance to expiratory flow and therefore expiratory wheeze, and associated (polyphonic) rhonchi on auscultation. Second, as we have already seen in Ch. 1, all that wheezes is not necessarily bronchospasm. This is because the terminal bronchioles can also be narrowed by secretions within their lumen (from super-imposed bacterial infection for example) or from oedema within their walls (e.g. from acute bronchiolar inflammation

typical of some viral infections; also from raised pulmonary venous "back-pressure" in some patients with left heart failure and pulmonary venous congestion - see above).

A third point relating to the mechanics of acute "asthma" is that the level involved can at times be the very small airways (1 mm diameter or less), and there, velocity of flow is low even normally (because of widespread prior branching and correspondingly increased total cross-sectional area for flow at this level). Correspondingly, narrowing of these airways may produce no wheeze at all. In this form of asthma, the chest may be "silent", so be on the look out for this in any hypoxaemic patient struggling to breathe (especially a child). One helpful sign here is pulsus paradoxus which can arise because the much greater increase in inspiratory effort produces a much more negative inspiratory intra-thoracic pressure. Test for this by checking the systemic pulse variation during respiration in suspected significant asthma.

Most mild acute bronchial asthma is not difficult to diagnose, but you sometimes have to put the patient under load to bring it out. At rest, one of the best tests is a comparison of the forced expiratory volume with the (unforced) total vital capacity - because of air trapping with forced expiration, this is less than 60% in asthmatic attacks. However, some patients only get wheeze early in the morning or after exercise and they must be diagnosed and monitored by measuring there own forced peak expiratory flow rate using their own mini-peak flow meters.

The important message from this section is that all that wheezes is not asthma and that asthma does not always wheeze.

The characteristic blood gas changes of acute asthma cannot be discussed until after our section on ventilation/perfusion matching/mismatching.

(b) The mechanics of chronic obstructive airways disease

As in the acute phase, when there is chronic or prolonged and gradually increasing obstruction of the airways, this will again produce an increased resistance to expiratory flow within the intrathoracic airways, and hence hyper-inflation of the chest, but this will now be seen even in between any acute attacks, and be manifest as a change in the shape of the chest, i.e. "barrel"-shaped chest (increased A-P diameter), kyphosis, also less than one fingers-breadth of trachea above the sternal notch, and hyper-resonance of the chest on percussion. As in acute obstruction, this hyper-inflation of the lung tends initially to be compensatory, (by increasing the elastic lung recoil during expiration), but unfortunately this happy state does not continue, because with persistent stretch and progressive alveolar degeneration in the chronic state, lung elasticity gradually tends to be lost, so that further hyper-inflation must occur, and this eventually reaches its limit. Moreover, it causes gradual flattening of the diaphragm, and this in itself provides an added problem because the diaphragm is normally in a position of maximum mechanical advantage as a pump-handle, and flattening from hyper-inflation compromises this. It therefore becomes common in chronic obstructive airways disease to find people trying other ways of overcoming things, e.g. putting on a "backing-pressure" (through pursing

their lips during expiration) though as we have seen, this method of compensation also has limitations.

So much for the background of ventilatory mechanics and the way they may help understand obstructive airways disease, but we still have paradoxes. In particular how can we talk about hyperventilation in cases with obstructive airways disease. You will commonly hear this said, but it is a real paradox. Also, how can we understand those cases of obstructive airways disease that do not have the predicted CO2 retention (many of them actually have a reduction in arterial pCO2!) To understand these aspects, we must now address the concept of ventilation/perfusion (V/Q) balance/ imbalance or matching/mismatching.

HYPERVENTILATION & VENTILATION/PERFUSION MISMATCHING

To introduce the subject, let us take the case of hypoxaemia at high altitude.

Here, hypoxaemia stimulates respiration (via the carotid bodies and at levels of arterial PO2 below about 60 mm Hg), so that ventilation increases not initially with any feeling of shortness of breath. This alveolar hyperventilation does not have much affect on the arterial oxygen saturation however, for several reasons. First, although there is some gradient between the ambient air outside the body and alveolar oxygen tension, it is not great. Even at ground level, on room air (PO2 approx. 150 mm Hg) it is hard to increase alveolar pO2 much above 120 mm Hg no matter how much one increases ventilation (because of the mandatory partial pressure occupied in the alveolus by CO2, N2 and water vapour). Second, with mild hypoxia there is very little reduction in arterial haemoglobin oxygen saturation (Hb is 90% saturated at pO2 60 mm Hg), so that any increase in alveolar pO2 will have very little effect to increase arterial blood oxygen content, which is what matters in terms of tissue 02 delivery. By contrast, this alveolar hyperventilation is very effective in bringing about a reduction of arterial pCO2, both because of the steep nature of the CO2 dissociation curve from blood with altered pCO2, and its free diffusibility through the alveolo-capillary membrane. This allows ready washout of CO2 from blood to levels well *below* normal. Thus, the overall blood gas response to high altitude is not just the expected reduction in arterial pO2 but a greatly reduced arterial pCO2.

Ventilation/perfusion matching.

Normally, ventilation and perfusion are fairly closely matched throughout the lung. We know of two mechanisms causing this. First, whenever there is a tendency within the lung for local arterial pO2 to fall, there is reflex pulmonary arteriolar constriction to that area, effectively shutting down the blood supply to any alveoli which happen to be under-ventilated. Contra-wise, local hypocapnia (low pCO2) in the alveolus leads to reflex local bronchospasm to shut down the bronchioles supplying the area. This sort of process is called upon to some extent under normal circumstances, for example with altered posture altering pulmonary venous back pressure to different areas of the lung and with it

local pulmonary blood flow. Ventilation/perfusion is not normally tightly matched in the upright posture, but because of the fairly large margin for error, this does not matter greatly - except when we come to pulmonary disease, of either the obstructive airways or interstitial type. Let us look first at the more difficult case, namely obstructive airways disease.

Airways Obstructive Disease and Blood Gases

If we obstructed the trachea, then the obvious result would be a failure of gaseous exchange both of CO_2 and O_2, so that arterial pCO_2 would rise and arterial pO_2 would fall. This still holds with partial obstructions of the trachea, and is also seen with inhibition of hind-brain respiratory centre drive by drugs, as well as with chest muscle paralysis. But with more peripheral airways obstruction (as in bronchial asthma) a peculiar thing happens in that although the arterial pO_2 does fall in the way we expect, there is characteristically a decrease rather than the expected increase in arterial pCO_2. This is usually explained in terms of "ventilation/perfusion mismatching with compensatory hyperventilation," but true hyperventilation seems incompatible with obstruction, and in any event how can hyperventilation (over-)correct arterial pCO_2 without correcting the hypoxaemia - after all there is nothing wrong with the alveolar exchange of blood gases in obstructive airways disease. A lot of current explanation is obscure and merely descriptive. My own view is that in obstructive airways disease, there is *patchy* obstruction affecting different areas of the lung differently, and having an effect which can be explained by reference to the following simple model of the lung:

Let us imagine that the left lung is a single alveolus whose ventilation is obstructed but whose perfusion remains entirely intact; and that the right lung is a similarly single but relatively unaffected alveolus with normal gaseous exchange. In the left lung, the reduced ventilation will produce a reduction in alveolar pO_2 and an increase in alveolar pCO_2. Blood coming to the left pulmonary capillaries from the left pulmonary artery will equilibrate with this, so that the left pulmonary venous blood draining back to the heart will have an increased pCO_2 and a reduced pO_2. However, this will then be mixed with normally-exchanged pulmonary venous drainage from the right lung, so that the degree of aberration in mixed pulmonary vein blood gases will be somewhat less than otherwise. When this blood passes through the systemic arteries to reach the head, respiration will be stimulated both by the reduced arterial pO_2 (via the carotid bodies) as well as the increased pCO_2 (hind brain respiratory centres). Now, this stimulated respiration will not be of much help in improving ventilation to the left lung (where airways resistance is already high), but in the normal right lung it will increase alveolar ventilation, and this will have an effect to wash out CO_2 from the blood, so that the pCO_2 in the pulmonary veins draining the right lung will now become much lower than normal, particularly given the steep dissociation curve of CO_2 from blood with varying CO_2 partial pressure. On the other hand, as discussed above with high altitude effects in normal subjects, the increased ventilation to this normal right lung will not much increase its alveolar pO_2 much at all. As a result, although the mixed venous blood (draining the combined pulmonary circuit), and therefore the systemic arterial blood, will continue to remain hypoxic, arterial pCO_2 may quickly come back to normal (through a combination of high pCO_2 from the left lung, plus a low pCO_2 from the right because of its hyperventilation). Actually, because the (hypoxic) drive to respiration continues, the amount of CO_2 washed out from the blood passing through the right lung may exceed that retained

by the left, so that the total mixed pulmonary venous pCO2 falls *below* normal. Moreover, this greatly increased ventilation of the right lung may determine that overall or total respiration (litres/min) may be increased.

Coming back to acute obstructive airways disease (e.g. bronchial asthma, acute bronchiolitis) and to a more realistic view of the lung as being composed of multiple segments, we can now begin to understand, first how the normal response to this obstructive airways condition can be an overall hyperventilation, and second how it may give rise to hypoxaemia associated not with CO2 retention, but a low arterial pCO2. However, we can only do this if we take the view that acute "asthma" is normally a *patchy* process throughout the lung, with some relatively normal segmental areas being hyperventilated and well perfused to (over-)compensate for other areas poorly ventilated but with continuing reasonable perfusion. An important corollary is that if we find that any individual patient's arterial pCO2 begins to rise, then we can say that the obstructive process is becoming very widespread and is serious, with few relatively normal areas left to compensate arterial pCO2 in this way. This is what we mean when we say that arterial pCO2 elevation in obstructive airways disease is an indicator of "alveolar hypoventilation". As a bald statement that may look strange, but what we really mean is that the:

Arterial pCO2 is the indicator of Overall EFFECTIVE alveolar ventilation.

The above is an important example because it shows how looking for signs of CO2 retention can help tell when a patchy and perhaps initially mild obstructive airways disease is becoming more generalized, severe and serious. At this late stage, there is indeed what amounts to total airways obstruction and the patient is in will grave danger from increasing hypoxia and CO2 retention. Mostly, in acute obstructive airways disease, low arterial pO2 is the problem, not CO2 retention, and the patient will usually respond to an increase in inhaled O2. But this may not much alter the underlying pathophysiological process, so watch for the signs of increasing elevation of arterial pCO2. If there is the slightest doubt, and especially if your other drug therapy is not working, then the patient must be artificially ventilated.

There is another aspect of drug treatment in obstructive airways disease to emphasize, namely that although we have very good drugs for producing bronchodilatation in patients with airways obstruction (e.g. salbutamol), these are not yet entirely specific and indeed theophylline may also have an effect to dilate the pulmonary arterioles. If in some areas they are more effective on the latter than the former, they may not be very effective overall, in that it may improve perfusion in some obstructed areas more than ventilation, and effectively produce a local shunt. In practice this is not usually a problem, but the principle is important. Other drugs may have an effect on cardiac output, so you must assess this as well as the arterial pO2, pCO2 and haemoglobin, clinically, in managing acute emergency pulmonary problems.

Chronic Obstructive Pulmonary Disease (COPD)

This raises another dilemma, because some patients follow our newly-explained blood gas pattern (low arterial pO2 together with low arterial pCO2) whilst others give what we originally predicted of obstructive airways disease, namely low arterial pO2 and high arterial pCO2. How do we explain these two extremes, the former being the so-called "pink puffer" and the latter the "blue bloater"? The clue, I think, is that most patients start off at the first end of the spectrum and gradually progress to the second. And this can now be explained by the above. Thus, we would expect the "pink puffer" to have patchy airways disease so that he could compensate for any tendency for CO2 retention (but not hypoxia) by hyperventilating remaining relatively normal areas of lung. The "pink puffers" often have an increase in total ventilation (litres per min.), but their difficulty with expiration is clinically obvious, and can be confirmed by a reduced peak expiratory flow rate. At the other end of the spectrum, towards which the "pink puffers" gradually to progress, are the "blue bloaters" who have more generalised disease and signs, with corresponding CO2 retention as well as hypoxaemia.

The severe hypoxaemia, in turn, causes severe generalised pulmonary arteriolar constriction (as a now-futile attempt at compensation) leading to pulmonary hypertension, and this plus increasing secondary hypoxic polycythaemia (with increased blood viscosity) leads to right heart failure - the right ventricle just cannot stand a high after-load despite hypertrophy.

So in most patients, what we see is merely a different part of the spectrum of chronic obstructive airways disease, the one progressing to the other. Nonetheless, along the way, some patients have much more pulmonary hypertension and subsequent right heart failure than others for any given level of arterial pO2. Some such patients drop their arterial pO2 profoundly at night (probably from sleep apnoea), and this is associated with nocturnal pulmonary hypertension, and eventually again, right heart failure.

In patients with acute obstructive airways disease, it is important to give oxygen. And therre is no problem with this in the "pink puffer" type of COAD. By contrast, giving high concentrations of oxygen to patients with acute exacerbations of C.O.A.D. and CO2 retention, can be dangerous, because by correcting the oxygen deficit, it can remove totally the hypoxaemia (chemoreceptor) drive to respiration and allow CO2 levels to just go on rising. In such cases, give supplemental O2 carefully, watch carefully for clinical signs of CO2 retention, and measure arterial pCO2 direct. Moreover, give supplemental oxygen gradually, initially 24%, and monitor arterial blood gases, gradually increasing the % inspired O2 until you achieve an optimal level of both arterial pCO2 and pO2.

Such monitoring can be very important even when you believe you have things under control, particularly in the acute-on-chronic situation.This is because body stores of oxygen are held almost entirely in the blood, whereas stores of CO2 are more in the tissues (largely in the form of bicarbonate). Thus, if we take a case of treating a patient with severe acute-on-chronic C.O.A.D. by artificial ventilation with a face mask O2, the arterial pO2 will normally rapidly adjust to the improved alveolar pO2 within minutes; but arterial pCO2 will take much longer because of the continued liberation of large quantities of tissue CO2 (converted from HCO3) into the circulation; this, together with the steep dissociation curve of CO2 from blood, means that vast quantities of CO2 can be

delivered to the lungs, and given up into the alveoli before a new equilibrium is achieved (about 1/2 hour). One might think that this CO2 could readily be blown off by the hyperventilation, but even in normal subjects there is a limited amount of space in the alveolus so that the total pressure must accommodate the sum of the partial pressures of O2, CO2, N2 and H2O. Now, N2 and H2O are not exchanged in the lungs, so the relative partial pressures of O2 and CO2 must make up the sum of the remainder. Therefore, if CO2 is suddenly delivered up in great quantities in this state, the alveolar and therefore arterial pO2 will not rise as much as you predict from your knowledge of the inspired PO2, and the patient may remain hypoxaemic for some time. This leads us to an important equation, namely:

Alveolar pO2 = Inspired pO2 - Arterial pCO2 divided by RQ

* Normally inspired pO2 = 150 mm Hg at sea level.

* RQ = Respiratory Quotient. For the sake of simplicity, say RQ = 1. Actually it is normally more like 0.8.

This emphasises how alveolar pO2 (and hence arterial pO2) is always limited by the amount of CO2 in the alveoli as a proportion of partial pressure at any one time.

As an approximation,:

The sum of alveolar pO2 and pCO2 is 150 mm Hg on room air.

OTHER AIRWAYS DISEASE

Interstitial Lung disease e.g. "interstitial pulmonary fibrosis".

This is often associated with hypoxaemia, but also, oddly, with hypocapnia. It was once thought that this latter was due to an "alveolo-capillary block", with the lesser diffusibility of oxygen across that membrane giving rise to a reduced arterial pO2 but no elevation of pCO2. This does occur to some extent, but the major problem is again one of alveolar ventilation/perfusion mismatching. Such conditions as "diffuse interstitial pulmonary fibrosis" remain patchy until late, so that relatively normal areas are able to make up for the CO2 retention (but not the hypoxia) generated in abnormal ones. Here, the diseased areas are involved in a process causing thickening of the alveolo-capillary membrane of the lung rather than an obstructive airways problem. That thickening does cause greater problems with O2 exchange than CO2, but more importantly, exudation of fluid or distortion/ lack-of-surfactant with collapse of the alveoli leads to an effective shunting of blood across that area of lung. As before, the CO2 retention brought about in such diseased areas can be more than

compensated for by hyperventilation within relatively normal lung tissue elsewhere, but the hypoxaemia cannot.

In interstitial lung disease not only is vital capacity reduced but also lung compliance, and hence these conditions are also referred to as restrictive lung diseases. In addition, transfer of gases like oxygen (the one we test with is carbon monoxide) is reduced because of the thickened alveolo-capillary membrane. This is a useful test in diagnosis, and in following patients' response to treatment, but it should only be viewed in relation to vital capacity (if vital capacity is down - as it will be even in obstructive airways disease - we will expect a reduced CO transfer; it is the ratio which is important).

Restrictive diseases include not only "diffuse" interstitial lung fibrosis, but also rib cage disease. You might think that rib cage disease, particularly of a generalised nature, such as may occur with ankylosing spondylitis, would cause CO2 retention, but some areas of lung can stilll expand more than others to normalize CO2 This makes the point that one can effectively hyperventilate even when the vital capacity is reduced, by increasing the rate of respiration. Thus, it is not until the late stages of even restrictive lung disease that CO2 retention is seen, whether that restrictive disease be due to interstitial fibrosis or rib cage disease.

The clinical clues to the restrictive airways disease are an obvious reduction in vital capacity. Pulmonary infiltration in the acute inflammatory stage is typically associated with inspiratory crepitations. Sputum examination can show neutrophil polymorphonuclear leucocytes. On the other hand, in granulomatous conditions (e.g. sarcoid), the sputum often contains more chronic imflammatory cells, such as lymphocytes and macrophages.

Pulmonary embolism

This is where a segment of lung suddenly loses perfusion but remains ventilated. The expected effect would be an increase in alveolar dead space, i.e. a segment of lung is now being ventilated but not perfused. We would not expect this to make too much difference to arterial blood gases.Compensatory hyperventilation of the remaining lung might produce a slight fall in arterial pCO2, but arterial pO2 should not change. Surprisingly, though, what we usually find is a fall in both arterial p02 and pCO2, which is not at all explained. This is much more characteristic of intra-pulmonary shunts, and not at all what we think is happening in pulmonary embolism, where an area of lung is not perfused area but is still ventilated. Perhaps when a pulmonary artery branch is obstructed, there is indeed a shunting of blood through abnormal collateral pathways around the effected area and not in close contact with alveoli, with the net effect of passaging some blood through areas not effectively ventilated. If this were so, we could understand how hypoxaemia could be produced and become the stimulus for hyperventilation of relatively normal lung areas elsewhere, to reduce overall arterial pCO2 as above. This would also be in keeping with the difficulty of improving arterial haemoglobin oxygen saturation oxygen in this condition. Nonetheless, the blood gas picture of acute pulmonary embolism is strange.

Despite our difficulty, there is no doubt that the characteristic (nuclear medicine scanning) evidence of pulmonary embolism is the presence of areas of lung which are well ventilated but not perfused, at least in the early stages. Later, of course, pulmonary embolism may progress to pulmonary infarction, and at that stage there may be no ventilation or perfusion of that particular segment i.e. a return to V/Q matching between the two. Therefore when you obtain a V/Q report that there are multiple perfusion defects throughout the lung with matching defects in ventilation, the primary condition may still be pulmonary embolism, but one which has progressed to infarction with the alveoli now stuffed full of blood, as well as absent perfusion, and hence to no ventilation perfusion mis-match.

Rules of thumb.

Arterial pCO2 reflects overall alveolar ventilation.

Arterial pO2 reflects overall alveolar perfusion.

FUNCTIONAL DIAGNOSIS: OTHER ASPECTS

Note that any cause, respiratory or otherwise, of chronic hypoxia can lead to secondary polycythaemia over time. This is initially compensatory (allowing as it does a greater amount of oxygen to be carried by each unit volume of blood), but it can eventually lead to problems. The increasing polycythaemia can gradually lead to increased blood viscosity, so that the blood becomes more difficult for the heart to pump, with precipitation of cardiac failure.

AETIOLOGICAL DIAGNOSIS

Chronic obstructive airways disease is importantly linked to cigarette smoking. But emphysema is also predisposed to by alpha-1- anti-trypsin deficiency, so think of this when patients present with this condition at a relatively young age. Chronic bronchial asthma also occasionally leads to chronic obstructive airways disease.

MCQs: MECHANISMS IN DISEASE

A. Mechanisms in Disease

The following would be characteristic of an acute classical bronchial asthmatic attack of moderate severity in a previously normal child.

1. Arterial haemoglobin oxygen saturation would tend to be be reduced.

2. There would typically be evidence of overall alveolar hypoventilation.

3. Arterial pCO2 would typically be reduced early on.

4. Characteristically, expiratory rhonchi or wheezes would be heard on auscultation of the lung.

5. Any "wheezes" would typically reflect underlying bronchospasm.

6. Yellow sputum, even in the absence of fever, would identify an underlying bacterial infective cause for the condition.

7. If the attack became severe, wheezes may no longer be heard.

8. In a severe attack, there may be a systolic arterial blood pressure rise during inspiration.

9. With a haemoglobin of 16 g/dl, an arterial pO2 of 40 mm Hg would be associated with a circulating level of unsaturated haemoglobin of approximately 8 g/dl.

10. Secondary polycythaemia is to be expected.

Answers at the end of chapter.

CLINICAL PROBLEM SOLVING

The next, and more important type of MCQ is the problem-solving one, where you need to first build up a diagnosis from the clinical information beforehand.

Solving the problem. Do this **using either the tutorial on Shortness of Breath** within this system,**or** by yourself with **paper and four columns drawn up as discussed already.** If you chose to do the latter, there is a **graphic solution in the next section** for comparison. But, either way, first read the following:

Clinical Diagnostic Problem-Solving. (You may now prefer to go onto the Online 'Shortness of Breath' tutorial.)

A 53 year old (1) garage mechanic (2) presents with a one week history of increasing cough, yellow sputum (3) occasionally streaked with blood (4), fever (5) and shortness of breath (6) associated with wheeze and especially difficult expiration (7). There has been no chest pain (8) or recent loss of appetite (9). On direct questioning, he admits to having become gradually but increasingly short of breath over the past 15-20 years (10), first only on moderate exertion such as hurrying up hills, but in the last year or two on relatively mild exertion such as climbing a single flight of stairs (11). The history has been punctuated by similar acute episodes as the present (12), and as in this attack, many seem to begin soon after catching a "cold" (13). Apart from this he has been relatively well in between times (14) with very little cough, except in the early morning when he usually brings up a little whitish sputum first thing (15). He attributes this to a "smoker's cough" (he has smoked 20 cigarettes per day since the age of 19) (16). General systems enquiry: no complaints except for some weight loss over the last few years (approximately 6 kg) despite a maintained appetite (17). Past History: no other important illnesses, in particular no childhood asthma or other allergic diseases (18). Family History: father died aged 62 of "emphysema", and his brother of apparently the same cause aged 54. Both were "moderate" smokers (19). There is no family history of allergic disorders such as asthma (20).Social History: no particular stresses (21). He admits drinking a "moderate" amount of alcohol (one-two cans of beer/day) (22). Drug therapy nil (22a).

Examination reveals a thin man (23) obviously short of breath and with an expiratory wheeze (24). There is a bluish facial flush (25). Temperature 38.5 deg.C (26) and slight mental confusion (27). Hands well perfused (28) but appear blue in comparison with the examiner's, as does his tongue (29). An occasional "flapping" tremor occurs when the outstretched hands are observed with hyper-extension at the wrists (30). Pulse 120/min, somewhat irregular (31), full volume and "bounding" (32). Blood pressure 160/85 mm Hg (33), JVP elevated 6 cm (34), with normal "a" and "v" waves (35). The cardiac apex beat is difficult to define (36); heart sounds normal (37), but there is an added third heart sound best heard in the epigastrium (38). No murmurs audible (39). In the abdomen no organs palpable, no ascites. In the periphery, there is slight bilateral ankle oedema (40) and in the optic fundi there is slight papilloedema with marked distension of the retinal veins (41).

Chest Examination: trachea midline but only one finger's-breadth is palpable above the sternal notch (42). On inspection, respiration is relatively rapid (30/min) but somewhat shallow and with a relatively long expiratory phase (43). The patient has a kyphosis and a rather "barrel"-shaped chest with an increased antero-posterior diameter (44). Percussion note hyper-resonant in all areas (45) except for dullness ay the left parasternal region anteriorly (46). Chest expansion poor (47). Peak expiratory

flow rate 120 litres/min (48) (Normal > 500 for age). Auscultation: two broad findings. First, reduced intensity (vesicular) breath sounds over most of the lung, associated in the mid to lower zones posteriorly with late inspiratory "crackling" crepitations bilaterally (49), and more widespread generalised polyphonic "wheezes" (50), most marked during expiration (51). Second, corresponding to the area of dull percussion note over the left parasternal edge, increased breath sounds of bronchial quality with fine late inspiratory "crackles", but much less in the way of rhonchi (52). Sputum thick yellow/green sputum; microscopy shows numerous neutrophils (53), and Gram stain, mixed organisms (54).

Approach to diagnostic problem-solving

If you have grasped the essence of the four-category approach to diagnosis from the previous chapter, you may wish to work through this problem without reference to the tutorial system. If so, you can then compare your solution either with that in the online tutorial on Shortness of Breath, or go to the graphic solution in the next section of this chapter. If the latter, the graph is best viewed by first centering it with the space bar underneath.

Either way, the following are **particular points** to note:

1. Information transfer between columns. Thus, blood in the sputum (4) is appropriately designated initially only to the Pathology column, but since the sputum is blood streaked, this suggests involvement of the upper airways, and so this information can also be put in our first or Anatomical column. In a similar way, much of the (6,7,43,50,51) in the Functional column leads to the conclusion that there is bronchiolar involvement (narrowing), i.e. allows the conclusion "bronchiolar" to be transferred to the first or Anatomical diagnostic column, and 'narrowing' to the Pathological column. Similarly, the left parasternal chest findings in the Functional column point strongly to involvement of the left lingula, and can be transferred to the Anatomical column. But beware of transferring information to the Anatomical involvement before you know that it relates to primary rather than secondary anatomical system involvement. Thus, under point No. 40, mild right heart failure is probably a secondary consequence of pulmonary hypertension following hypoxaemia, and best left in the Functional column. Reserve the 'Where' column for conclusions relating to the primary site of anatomical problem.

2. Interim Conclusions. When appropriate, 'rule off' and draw interim diagnoses in all of the four categories. Always do this whenever there is a change in the rate of progression of any important symptom or symptoms, e.g. when a chronic symptom develops a recent exacerbation, or if it suddenly worsens in a dramatic way. This is very helpful in the making the overall diagnosis, because it allows you to summarize all four aspects of the diagnosis as the case unfolds over time.

Solve the problem in this way, and then answer the following MCQs.

WHICH OF THE FOLLOWING ABOUT THIS PATIENT IS/ARE CORRECT?

1. The history suggests that this man's underlying pathological condition is carcinoma of the lung.

2. The pathological diagnosis of the recent condition is an acute bacterial inflammation involving the bronchioles.

3. There is good evidence of bronchospasm in this man.

4. There is evidence of chronic obstructive airways disease.

5. The left parasternal signs are situated in the medial basal segment of the left lower lobe.

6. The signs at the left sternal edge are characteristic of collapse associated with an obstructed bronchus.

7. Given a haemoglobin of 16 g/dl, you would not be surprised if his arterial pO2 was < 60 mm Hg.

8. There are now clinical signs indicating an elevated arterial pCO2.

9. The presence of papilloedema necessitates an immediate CT scan of the brain.

10. This man should be given at least 40% oxygen to breathe.

11. Alcohol has played a significant role in this man's underlying disease.

12. Cigarette smoking has probably contributed significantly to this man's background illness.

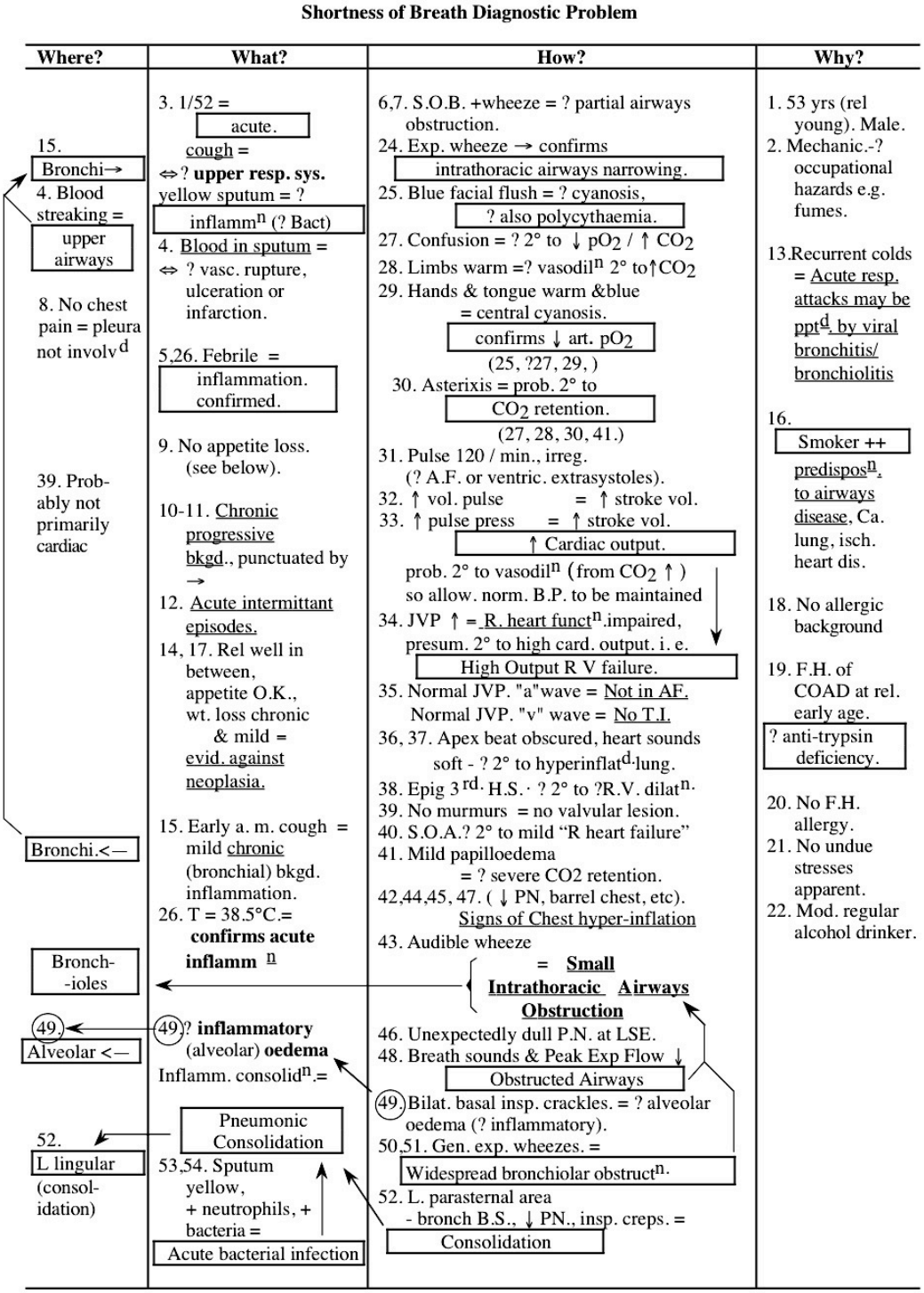
13. Alpha 1 anti-trypsin deficiency is a possible background predisposing cause for this man's chronic condition.

14. There is evidence of right heart failure.

15. There is evidence of left ventricular hypertrophy.

16. The irregular pulse is most likely due to atrial fibrillation.

PROBLEM SOLUTION: GRAPHIC-1



PROBLEM GRAPHIC: 2

CONCLUSION.

Shortness of breath Diagnostic Problem (continued)

Anatomic Diagnosis	Pathological Diagnosis	Functional Diagnosis	Aetiological Diagnosis
1. Airways Disease	Chronic progressive.	Obstructive, with 2° hypoxaemia on exertion. Prob. also 2° polycythaemia.	Smoking. ? also alpha 1 anti-trypsin deficiency
2. Bronchi	Chronic mild inflamm^{n}.	2° cough.	Long-term smoking.
3. Bronch-ioles.	Acute superimposed episodes of bacterial infection.	Wheeze 2° to resistance airways narrowing.from inflamm. oedema.	Ppt^{d}. by viral resp infection.
4 (a). Upper resp. tract. (Bronchial)	Acute infection, with vascular congestion & 2° cap. rupture	Cough, yellow sputum, & mild haemoptysis.	Ppt^{d}. by acute viral resp. infection.
4(b). Bronch--iolar (wide--spread)	Acute (1/52) (bacterial) infection.	Inflamm. oedema → obstruction with (i) 2° wheeze, hypoxaemia, & severe hypercapnia. (ii) 2° R. heart failure (at least partly related to ↑ CO_2, i. e., high output failure, ? also in part 2° to ↓ pO_2 causing pul. hypertension → ↑ afterload R. H. F.).	As above.
4(c). Alveolar (basal)	Acute infection	Aggravating S.O.B.via (i)pul. congestion → ↑ lung compliance, and (ii) exudative oedema → ↓ alv. gas exchange.	As above.
4(d). Lingula	Acute infective (pneumonic) consolidation.	Aggravating S.O.B. by effectively causing an area of shunting i.e. perfusion of an area of lung no longer being ventilated.	As above i.e. viral → bacterial infection.

PROBLEM: DIAGNOSTIC DISSERTATION

Diagnostic Dissertation: This should be at the end and clearly demonstrate the logic of your conclusions and, through your knowledge of pathophysiology, show the unfolding 'chain of mechanism' over time (e.g. acute infective exacerbation of chronic obstructive airways disease with secondary hypoxaemia and pulmonary arteriolar constriction leading to pulmonary hypertension, right heart failure, right heart dilatation and tricuspid valve incompetence).

Example: Diagnostic dissertation re the present problem: This 53 year old man presents with a longstanding and gradually increasing shortness of breath, the pathological basis of which is unlikely to be carcinoma in view of the duration, so is probably a more degenerative process. Anatomically there is evidence of chest hyperinflation consistent with obstructive airways disease. Functionally the disease has progressed in severity to cause chronic underlying limitation of exercise tolerance. Aetiologically, his cigarette smoking is likely to be important, but the relatively early onset of the condition in this man, together with his family history of "emphysema" make one wonder whether alpha1 antitrypsin deficiency might also be contributing. There is no evidence that his obstructive disease has an allergic aetiological basis.

Acute intermittent episodes over the years: most likely viral upper respiratory tract infection, gradually spreading to involve the bronchi and, from the functional viewpoint, the bronchioles, and probably narrowing them by causing bronchiolar mucosal oedema so as to exacerbate the degree of airways obstruction for a time.

Acute episode developing from week before admission : Pathologically, there is clear evidence of infection. Blood streaking of sputum suggests upper airways involvement anatomically, but functionally more important from that viewpoint are the bronchioles (increasing shortness of breath and expiratory wheeze). On examination, that wheeze and therefore the acute exacerbation of airways obstruction is widespread. Basal inspiratory crepitations suggest acute inflammatory alveolar oedema as well. The functional consequences are severe, including hypoxaemia (blue warm hands) and most probably hypercapnia (increased pulse rate, "bounding" pulses, wide pulse pressure, warm hands, metabolic flap, confusion, slight papilloedema, marked distention of retinal veins). There is also evidence of right heart failure (third heart sound in epigastrium reflecting cardiac dilatation, JVP elevated, some ankle oedema). This has probably resulted from hypoxaemia causing pulmonary arteriolar constriction and pulmonary hypertension, right ventricular pressure overload, and subsequent right ventricular dilatation and impairment of right heart function.

Localised process in left parasternally: The signs at the left parasternal edge are characteristic of consolidation, pathologically, within the left lingula anatomically. Their degree of contribution to the impairment of respiratory function is difficult to judge, but such consolidation could produce an area of perfused but not ventilated lung, i.e., a shunt, and this could certainly exacerbate hypoxia, (less so hypercapnia).

Suggested investigations: Micro. and Gram stain of sputum, also culture. Blood cultures in view of fever. Blood gas monitoring, during cautious oxygen replacement (in view of hypercapnia). Chest x-ray to confirm airways disease and lingula consolidation, and to exclude any pneumothorax (unlikely on history, but important). Full blood count (? polycythaemia from chronic hypoxaemia; ? elevated neutrophil count with toxic changes reflecting significant bacterial infection).

Further investigation: for alpha1 antitrypsin deficiency.

Final conclusion: From the above, this man has had a chronic slowly-progressive process of (bronchiolar) airways narrowing and (secondary) alveolar hyperinflation, with an acute exacerbation of this process precipitated by a respiratory infection, which has led not only to increased bronchiolar narrowing (? from inflammatory oedema), but also to pulmonary parenchymal alveolar inflammation in the lower zones, especially in the left lingula which shows evidence of pneumonic consolidation. Functional impairment of respiration is now severe, with hypoxaemia, secondary pulmonary hypertension and right heart failure, together with carbon dioxide retention. The process is severe now, but has been moderately severe in functional terms for some time, as evidenced by increasing shortness of breath and probable polycythaemia (compensation for chronic hypoxaemia). Background caustion: anti-trypsin deficiency; cigarette smoking.

General Comment

Avoid the all-too-common pitfall of just naming diagnostic terms, especially early on. Thus many students will 'recognize' this patient as "a case of COPD." (chronic obstructive pulmonary disease). Now, this patient does have chronic airways obstruction but he has much more. Moreover, the general abbreviation "COPD" does not tell us anything about the functional degree of airways obstruction in *this* patient, where the widespread polyphonic wheeze allows the better conclusion: "Widespread bronchiolar narrowing." Nor did it tell of the obvious evidence of alveolar hyperventilation, or of right hearth failure. So don't let any general textbook "off-the-rack" diagnosis cloud your problem-solving in individual cases. They may be useful as a background, but background they should remain, at least until the very end, and always provided they are appropriate to the individual under consideration in every word and syllable, and with the important caveat that they should fully address all four categories of diagnosis.

MCQ ANSWERS

Answers to MCQs:

Mechanisms in Disease: 1,3,4,5,7, correct. All others false.

No 9. false: See section early on in 'Functional Diagnosis' in this chapter for expected Hb saturations with various levels of arterial O2. Thus, we can expect an arterial O2 of 40 mmHg to be associated with an Hb saturation of 75%, not the 50% suggested by this question.

Problem Solving MCQs: 2, 4, 7, 8,12,13,14 are correct. All others false.
No. 3 The wheeze in this man is much more likely due to bronchialar wall oedema from the inflammation than bronchospasm. After all, there is no evidence that he has bronchial asthma.

No 7. See section early on in 'Functional Diagnosis' in this chapter for expected Hb saturations with various levels of arterial O2. This man has central cyanosis, which we can certainly detect with an unsaturated Hb of 4g/l or 75% Hb saturaion. This occurs with an arterial pO2 of approximately 60 mm Hg.