CHAPTER 15 - ACID BASE DISTURBANCES

INTRODUCTION TO BIOCHEMICAL DIAGNOSIS IN DISEASE

In what follows we have to consider some areas where biochemistry is essential to diagnosis. Nonetheless, it remains important to keep our four diagnostic caegories firmly in mind.
1. Define what investigations you need only on the basis of where you are deficient within any of your four major categories of clinical diagnosis (Anatomy, Pathology, Function, Aetiology). Never fall into the sloppy habit of ordering 'routine' investigations. It is costly, mindless, unhelpful, and often confusing. So beware of doing 'gropograms!'

2. Only order investigations in the light of the clinical context in which problems arise.

3. In interpreting biochemical abnormalities, keep to the same approach of asking broad questions before detailed ones, just as you would with clinical diagnosis (e.g. if there is a raised plasma alkaline phosphatase, don't assume it to be of hepatic origin - ask first what organ system it came from e.g. it could be from bone, placenta or a liver source).

4. If intelligently used, biochemistry can help determine the various categories of diagnosis at the investigation level, in much the same way that physiology can help at the clinical one. Thus, biochemical tests can contribute not only directly to Functional diagnosis, but indirectly to the Anatomical one (e.g. liver alkaline phosphatase raised to more than twice normal suggests, in the appropriate context, not just liver disease, but bile duct involvement - see Ch. 13). Biochemistry can also contribute to our Pathological diagnosis, e.g. raised troponin suggests myocardial infarction rather than ischaemia.

ACID BASE BALANCE

The daily production of hydrogen ion is enormous (approximately 10,000-15,000 mmol). The vast majority of this (99.5%) results from cellular metabolism of carbon-containing compounds to CO_2 and water. Further metabolism of CO_2 is the formation (by red-cell carbonic anhydrase) of carbonic acid, which dissociates to hydrogen ions and bicarbonate ions, the former being buffered by the red cell haemoglobin until it reaches the lungs where a reversal of the reaction occurs, effectively eliminating all hydrogen ions delivered in this way (i.e. as CO_2 and H_2O).

Organic acids are not always disocciable at body pH of 7.4, which means that their H^+ ions cannot be metabolised via the carbonic acid pathway, H^+ plus CO_3^- <------> H_2CO_3, so they end up as non-volatile acids tending to cause blood acidosis. For example, lactic acid accumulates in conditions of hypoxaemia as the end-product of the glycolytic cycle. Non-volatile organic and inorganic acids which

cannot be converted to CO2 and water must be eliminated in the urine and such compounds include (H+ ---> 2H+) phosphate and uric acid in normal circumstances; salicylates (overdose), hydroxy-butyrate and aceto-acetate (diabetic keto-acidosis) in abnormal states.

The body has a huge capacity to buffer hydrogen ion so that blood pH is changed minimally under circumstances of acid or base overload. In the red cells, haemoglobin is the most important buffer, then plasma protein, and in other cells, phosphate and protein. Plasma and ECF bicarbonate are the most important sources of buffer against hydrogen ion excess. Bone also provides a potential reservoir of buffer though this is not readily mobilised and can only be of value in states of chronic acid/base imbalance.

Normal Blood Gases

Arterial blood: pO2 85-105 mm Hg; pCO2 38-44 mm Hg; pH 7.35-7.45 (average normal 7.40); arterial haemoglobin O2 saturation 95-97%; plasma bicarbonate 27 (24-30) m.mol/l.

Mixed venous blood: pO2 38-42 mm Hg; pCO2 42-49 mm Hg; pH 7.33-7.40; O2 haemoglobin saturation 70-75%.

Alveolar blood gases: normal pO2 90-115 mm Hg; pCO2 38-44 mm Hg.

A. RESPIRATORY ACID/BASE DISTURBANCE

Having dealt at length with respiratory O2 and CO2 abnormalities in chapter 2, we are now in a position to look at acid/base disturbances of respiratory origin.

Recall the relevant Henderson-Hasselbalch dissociation equation:

$$CO_2 + H_2O \text{ -------> } H^+ + HCO_3^-$$

1. **Respiratory acidosis**

(a) Acute respiratory acidosis - caused by acute alveolar hypoventilation (CO2 retention). Always assess the clinical situation, in particular whether you are dealing with acute respiratory disease or acute on chronic (? obstructive) airways disease (see Shortness of Breath chapter). When it comes to the interpretation of blood gases in acute cases the following is the important

Clinical acid-base guideline 1. Acute respiratory acidosis

pH will fall by approx. 0.07 units for each 10 mm Hg rise in pCO2.

The immediate associated rise in plasma bicarbonate is approx. 1 mmol/l for each 10 mm Hg rise in pCO2. Provided you bear in mind the clinical context, you can calculate from this whether the blood gas changes are entirely due to an acute respiratory acidosis, or whether there is something else superimposed.

Example: a previously-well patient is admitted acutely short of breath with the following arterial blood gases: pH 7.19; pCO2 74 mm Hg; pO2 35 mm Hg; HCO3 27.6 mmol/l. From the above, we can see that this pH, pCO2, and bicarbonate are entirely consistent with an acute uncomplicated respiratory acidosis. Any blood gas deviation from this value would suggest something else in addition. For example, if this patient had previous chronic obstructive airways disease, he might well have had an element of chronic respiratory acidosis to begin with and we will see how this may complicate the picture by some examples below.

(b) Chronic respiratory acidosis

The reason for the (small) rise of bicarbonate in acute respiratory acidosis is the immediate disturbance of the equilibrium between carbonic acid on one side of the Hendersen-Hasselbalch equation and hydrogen ion plus bicarbonate on the other. But if respiratory acidosis is maintained over hours or days, then renal compensation ensues to result in bicarbonate retention. This starts at about 10 hours, peaks at 18 hours and is complete by 3-5 days. N.B: this elevation of plasma bicarbonate is not the result of more avid proximal tubular bicarbonate reabsorption, which is maximum in any case, but due to the urinary secretion of hydrogen ions in the distal tubule; this hydrogen ion is formed from renal tubular carbonic anhydrase so leaving HCO3 for reabsorption, and thereby elevating plasma bicarbonate, and allowing acid excretion.

At this stage of compensation, we can therefore expect a much greater increase in bicarbonate for any given rise in arterial pCO2 namely:

N.B. Clinical acid-base guideline 2. Chronic respiratory acidosis

4 mmol/l bicarbonate rise for each 10 mm Hg rise in pCO2.

This compensated phase is also one of partial correction of pH, and we now predict:

A fall of only 0.02 units in pH for every 10 mm Hg elevation of arterial pCO2 above normal.

2. **Respiratory alkalosis**

(a) Acute Respiratory Alkalosis

Acute hyperventilation is the commenest cause, mostly secondary to acute anxiety or hysterical states. If a patient is hyperventilating in this way, we should not expect much increase in arterial pO2 (Ch. 2), but on the other hand hyperventilation is very effective in washing out alveolar and therefore arterial CO2. This will lower arterial pCO2 substantially, which in turn will drive the Henderson-Hasselbalch equilibrium,

$$CO_2 + H_2O \text{ -------> } H^+ + HCO_3^-$$

to the left. This will tend to lessen the CO2 fall but has the effect of mopping up hydrogen ions and producing alkalosis. Such an acute alkalosis produces a secondary reduction in ionised calcium, so that cramp, tetany, and tingling of the fingers and mouth may ensue to worry the patient further.

N.B. Clinical acid-base guideline 3

For every 10 mm Hg fall in arterial pCO2 in the acute phase of respiratory alkalosis, pH rises by approx 0.1 units and bicarbonate falls by approximately 2 mmol/l.

However, as subsequent examples will show, you must again be careful to interpret blood gases only in the light of clinical circumstances.

The following arterial blood gases would be characteristic of an acute respiratory alkalosis:

pO2 120 mm Hg; pCO2 20 mm Hg; pH 7.61; HCO3 21 mmol/l.

As these blood gases follow precisely our guideline, there is no need to look further if the clinical situation is in keeping with acute respiratory alkalosis.

Clinical point

At room air (78% N2), combined pO2 and pCO2 in the alveolus can never really exceed 150 mm Hg, so that hyperventilation is unlikely ever to produce an alveolar (and therefore an arterial) pO2 of greater than 120 mm Hg on room air (approx. 20% of 760 mmHg = 150 mmHg).

(b) **Chronic Respiratory Alkalosis**

If hyperventilation is maintained over a long period, renal compensation of pH ensues from retention of hydrogen ions and consequent lowering of plasma bicarbonate (the latter again merely being a secondary consequence of disturbance of the Henderson-Hasselbalch equation: $CO_2 + H_2O$ -------> $H^+ + HCO_3^-$). Again, the fall in plasma bicarbonate is not the result of inhibition of renal bicarbonate

reabsorption in the proximal tubule. Rather, there is a reduced hydrogen ion excretion as ammonium and titratible acid in the distal tubule, and it is this retained H+ which lowers serum HCO3-. And secondary to the reduced H+ excretion there is a relatively alkaline urine. This process is a compensatory one, i.e. it lessens the deviation of pH from normal, but at the expense of causing bicarbonate levels to fall further. Therefore, with chronic respiratory alkalosis:

N.B. Clinical acid-base guideline 4.

For every 10 mm Hg fall in pCO2 we can expect a fall of 4 mmol/l in HCO3, and only a .06 unit pH rise.

Plasma bicarbonate rarely falls below 15 mmol/l in a previously normal patient, though the situation may be different in patients with pre-existing disease, or with previous disturbance of acid-base balance, e.g. due to diuretic drug therapy causing previous metabolic alkalosis. As with respiratory acidosis, the way to resolve this is first to take a careful history and then examine the patient closely; secondly to see whether the pCO2, bicarbonate and pH changes are entirely consistent with a respiratory alkalosis of acute or chronic type. If not, then some other (metabolic) acid or base disturbance must be present.

Tthe tubular maximum of bicarbonate is changed in chronic respiratory alkalosis and acidosis (via chronic changes in pCO2), and in such a way as to facilitate the maintenance of a high plasma bicarbonate in chronic respiratory acidosis and a low one in chronic respiratory alkalosis.

B. METABOLIC ACID-BASE DISTURBANCES

1. **Metabolic Acidosis**

a). Acute metabolic acidosis

This is where acid accumulates in the blood from either endogenous cause e.g. renal failure (when normal non-volatile acid can't be excreted), diabetes (where fatty acids accumulate) or tissue hypoperfusion (where anaerobic metabolism leads to the accumulation of lactic acid); or from exogenous cause - e.g. salicylate overdosage (salicylic acid accumulation); ethylene glycol poisoning (metabolised to oxalic acid); methanol poisoning (metabolised to formic acid); and paraldehyde (a sedative) overdosage (metabolised to acetic acid). In metabolic acidosis, the increased hydrogen ion combines with bicarbonate to produce carbonic acid, so lowering plasma HCO3-. We might also expect that this increase in carbonic acid would, via carbonic anhydrase, increase production of CO2 (H2CO3 <--------> H2O + CO2) and therefore lead to an elevation in arterial pCO2, as an immediate effect. However, in practice we don't find an elevated arterial pCO2 at all, even in the early stages, but rather a decreased one, because the reduction in pH in metabolic acidosis is itself a sufficiently

powerful (medullary centre) stimulus to respiration to more than blow off the increased CO2 formed, thereby driving pCO2 below normal. This fall of arterial pCO2 is immediate; it is sometimes referred to as respiratory compensation, but it is not really this in the sense we usually refer to, namely as a secondary (e.g. renal) adjustment, even though it does have the effect of limiting the pH fall. So strong is the acidotic stimulus to respiration that patients with acute metabolic acidosis *should* have an arterial pCO2 *below normal*; if not, then there is alveolar hypoventilation from some respiratory problem (see Ch.2 - Shortness of Breath) i.e. respiratory failure needing artificial ventilation. This might occur, for example, in someone who develops acute diabetic ketoacidosis on a background of previous chronic obstructive airways disease.

N.B. Clinical guideline 5.

In uncomplicated acute metabolic acidosis:

For every 0.1 unit pH fall, arterial pCO2 will fall by about 8 mm Hg to a minimum of 14 mm Hg at pH 7.1. (Values of pCO2 higher than the predicted value represent alveolar hypoventilation i.e. respiratory failure).

Also, **for every 0.1 pH unit fall, plasma HCO3 will characteristically fall by approx. 8 mmol/l.**

b). Chronic metabolic acidosis

Clearly, in the more chronic state, the fall in pH will be lessened by hydrogen ion excretion by the kidney, particularly by the distal tubule in the form of titratable acid and ammonium ion, the latter being highly inducible and therefore very effective in compensating pH in chronic metabolic acidosis. However, our understanding of acid secretion by the distal tubule has changed somewhat in recent years. It used to be thought that glutamine in the distal tubule broke down to form ammonia (NH3) which was then available to buffer H+ ions and secrete them into the distal tubular lumen, where they were 'trapped' as (positively-) charged ions in the form of ammonium or NH4+. The problem with this is that the dissociation constant or pKa of the equilibrium between ammonia and ammonium occurs only at about pH 9, well above the pH of normal blood, so that the product of this reaction in vivo is mostly ammonium ion in any case. Ammonium excretion in the urine is indeed important in compensation of metabolic acidosis, but for the following different reason. Ammonium normally combines with CO2 in the liver in the process of ureagenesis according to the equation.

$$2NH4+ + CO2 <---> 2H+ + urea + H20$$

In chronic acidosis this equation is pushed to the left, so reducing the overall degree of acidosis. The sequence of events is that acidosis reduces the utilisation of NH4+ in the urea cycle, and thereby favours its utilisation in renal glutamine synthesis. This glutamine then acts as a store of ammonium ions from which NH4+ can dissociate and be excreted in the urine to increase blood pH. This

mechanism becomes increasingly important as time goes by, because the increased renal levels of glutamine induce high levels of glutaminase in the distal tubular epithelium, so further increasing the availability of ammonium ions (which of course contain H+) for renal excretion. Looked at in this light, renal glutamine synthesis is really a way of mopping up the excess ammonium (with its associated H + ions) induced by acidosis, and making it available for renal excretion.

Plasma potassium rises dramatically in metabolic acidosis secondary to the administration (e.g. overdose) of mineral acids such as ammonium chloride. due to two factors. First, H+ tends to move into cells to be buffered, and in return K+ moves out. Second, the distal renal tubular sodium reabsorption mechanism tends to use the excess plasma H+ to exchange for sodium reabsorption, so diminishing the amount of K+ excreted by this mechanism. This leads us to another important guideline viz:

N.B. Clinical acid-base guideline 6.

In acute metabolic acidosis we can expect a rise of approx. 0.6 mmol/l in plasma K+ for every 0.1 unit fall in pH.

(The opposite approximately holds in alkalotic states.)

Note that the above is much more typical in states where the acidosis is due to the presence of inorganic acids such as ammonium chloride or HCl than with organic acids such as lactic acid. The latter, being organic are much more readily able to cross the cell membrane and be excreted, so characterictically plasma K+ is much less disturbed. Lactic acidosis typically occurs with hypotensive shock, where lack of tissue oxygen prevents lactic acid from being processed to pyruvate etc. i.e. from entering the aerobic Kreb's cycle.

Clinical point.

There is an important exception to this general rule about organic acidosis.

In diabetic acidosis DIABETIC ACIDOSIS (keto-acidosis), plasma K+ does increase, and sometimes dramatically, but by quite a different mechanism from that associated with inorganic metabolic acidosis.

Tthe very high plasma K+ in diabetic keto-acidosis is largely brought about by the very low plasma insulin causing a reduction of the normal glucose-facilitated uptake of K+ by the cells. (See Chapter 17 for a more detailed discussion.)

Metabolic Acidosis and the Anion Gap

Normally, the sum total of the plasma Na+ plus K+, minus the two major negative ions Cl- and HCO3-, ranges between 10 and 19 mmol/l (anion gap). If the value is greater than 20, the difference must be due to some abnormal negative ion. In diabetes, this will be hydroxy-butyrate, aceto-acetate etc; in uraemia it will be the nonvolatile retained acids (phosphate etc.) An anion gap also occurs with exogenous overdose with acids, such as salicylic acid due to the salicylate ion itself. Most importantly, any large unexplained anion gap raises the question of hypoperfusion of tissues andlactic acidosis from anaerobic metabolism. Sometimes this can be quite subtle, especially in acute small bowel ischaemia from mesenteric thrombosis/embolism which may have few clinical signs. If your patient is hyperventilating in a situation where you suspect metabolic acidosis, measure not only arterial pH, but the

Anion gap, and where this **is more than 20, ask the lab. to measure blood lactate** as well.

2. Metabolic Alkalosis

(a) Acute Metabolic Alkalosis

May be seen with the administration of sodium lactate (where the lactate ion mops up hydrogen ions), but clinically most often produced by **vomiting**, i.e. HCl loss. The primary change in this situation is a rise in pH. Increased dissociation of carbonic acid (H2CO3) to bicarbonate and H+ tends to limit this.

As a result:

N.B. Clinical guideline 7.

Plamsa HCO3- increases by about 6 mmol/l for each 0.1 unit rise in pH, acutely.

Arterial pCO2 rises very little, approx. 0.7 mm Hg for each 1.0 mmol/l rise in HCO3-.

(b) Chronic Metabolic Alkalosis

Prolonged vomiting (acid loss) should, in theory, produce secondary hypoventilation with a compensatory increase in arterial pCO2 in an attempt to retain H+, but in practice this increase is often quite small and may not occur at all. Also, we should expect hydrogen ion to be retained by the kidney (alkaline urine) so minimizing blood pH elevation over time. However, metabolic alkalosis is often accompanied by the simultaneous occurrence of potassium depletion (especially in prolonged vomiting) which complicates the final acid-base picture. This potassium depletion arises not only from potassium loss in the vomitus, but from two other sources; first, by potassium going into cells in exchange for hydrogen ions coming out to buffer the metabolic alkalosis, and second, by the frequent

concurrent loss of sodium (chloride) in the vomitus which, through ECF volume depletion, stimulates aldosterone, and thereby evokes potassium loss in the urine as a price to pay for sodium retention. In the latter situation, severe potassium depletion can eventually occur, so that potassium ion is no longer available for exchange with the continuing avid renal DCT sodium re-absorption, and hydrogen ion now takes its place. Hence, sodium and potassium depletion concurrent with metabolic alkalosis can give rise to a

******** **Paradoxical acid urine in states of prolonged vomiting**, so that far from compensating for the blood alkalosis, the kidney response now makes it worse.

One of the commonest causes of chronic metabolic alkalosis we see is related to chronic (sodium and) potassium depletion from long term chronic diuretic therapy (e.g. thiazides) without adequate potassium replacement. You should readily be able to work out how this arises from the above discussion.

EXAMPLES, MCQs & PROBLEM SOLVING

(i) An 18 year old girl was admitted to the Emergency Departmet complaining of a 2 day history of increasing "pins and needles" in her lower legs together with increasing generalized weakness and difficult in breathing. She was thought to be hysterical, but blood gases were illuminating and illustrate how sometimes biochemistry can be used to correct a false clinical impression. The blood gases were as follows:

pH 7.3; arterial pCO2 60 mm Hg; arterial pO2 55mm Hg; bicarbonate 29 m.mol/l

We can calculate that this fits entirely with our criteria for an acute respiratory acidosis, and in a healthy girl with previously normal acid base status, this must be the diagnosis (pO2 also low). Actually, this girl turned out to have ascending infectious polyneuropathy (Guillain-Barre syndrome) causing weakness of the chest muscles and resultant hypoventilation; she needed emergency ventilation and not the brown paper bag re-breathing initially suggested to all by the clinical impression.

(ii) A 67 year old man is seen 24 hours after an operation on his prostate gland, during which a 'moderate' amount of blood was said to have been lost. On examination, he has extremely poor peripheral perfusion with cold, sweaty, cyanosed hands and feet, BP 80/60 mm Hg, pulse 130/min, JVP not detectable (even when lying flat). Arterial blood gases show the following:

pO2 80 mm Hg; pCO2 18 mm Hg; HCO3- 5.5 mmol/l; pH 7.1; Na+ 138 mmol/l; K+ 4.1 mmol/l; CL- 105 mmol/l.

Clearly, he has an acidosis (pH 7.1). If this were purely a respiratory acidosis, he would have a high pCO_2 (and if he had previous chronic obstructive airways disease it might still be high). Therefore, he has a metabolic acidosis, which has also caused a greatly (and appropriately) reduced plasma bicarbonate. The question is what has caused the acidosis. Calculation from the above shows an anion gap of more than 30 mmol/l. Diabetes, uraemia and salicylate intoxication could be readily excluded as a cause of this, and one would be very suspicious of is lactic acidosis from circulatory shutdown causing the tissues to metabolise largely anaerobically and so produce lactic acid. Indeed in this case, direct measurement revealed an increased level of blood lactate.

(iii) A man with long-standing chronic obstructive airways disease is admitted to hospital with a severe haematemesis. He returns to the Intensive Care Unit after gastric surgery, being artificially ventilated on pure oxygen with the following arterial blood measurements.

pH 7.62; pO_2 150 mm Hg; pCO_2 40 mm Hg; HCO_3^- 39 mmol/l.

On the face of it, this may look very much like an uncomplicated metabolic alkalosis (normal pCO_2, high bicarbonate and high arterial pH). However, this example emphasises the importance of interpreting blood gases only within their clinical context. This man has chronic obstructive airways disease, and therefore may well normally run a high arterial pCO_2 from alveolar hypoventilation. Certainly, if there is no reason to suspect metabolic alkalosis (e.g. diuretics, vomiting and/or hypokalaemia), the high bicarbonate could be explained by his previous chronic obstructive airways disease. If so, the pCO_2 might be too low for this man's usual state, and we would have to conclude that he had an acute superimposed respiratory alkalosis related to relative over-ventilation. Actually, this was indeed the case, because this man's blood gases prior to operation did show a chronic respiratory acidosis related to COPD, with a much higher arterial pCO_2.

(iv) An elderly diabetic with severe chronic obstructive airways disease is admitted to the Intensive Care Unit in coma. Initial arterial blood gases are as follows:

pH 7.08; pO_2 60 mm Hg; pCO_2 80 mm Hg; plasma HCO_3 23 mmol/l.

On the face of these initial blood gases, this patient might be thought to mostly to have an acute respiratory acidosis. However, because this episode occurred on a background of chronic obstructive airways disease, it was important to obtain previous medical records and look back at arterial blood gases in the stable state prior to admission. These revealed the following:

pH 7.36; pO_2 50 mm Hg; pCO_2 70; mm Hg; HCO_3 36 mmol/l.

With this knowledge, we can see that the bicarbonate is now far too low in comparison with his previous level, and that the very low arterial pH cannot at all be explained by the slight recent rise in arterial pCO_2 above his usual levels. This patient therefore has an acute metabolic acidosis super-

imposed on his previous usual chronic compensated respiratory acidosis. (He may have diabetic ketoacidosis, so examine for urine and blood glucose and ketones).

(v) Example of a Mixed Picture of Acid Base Disturbance

Patients with COPD (and cor pulmonale) are often put on diuretics, and this can give a mixed picture of a chronic respiratory acidosis (COPD) and chronic metabolic alkalosis (from the diuretic causing ECF volume depletion and hypokalaemia, and therefore excretion of H+ in the urine rather than potassium in exchange for avid sodium re-absorption in the distal tubule). Provided one takes the background into account, this can be readily worked out; thus both the bicarbonate and the pH will be higher than calculated on the basis of a chronic respiratory acidosis alone. Arterial blood gases in this situation might be:

pH 7.4; pO2 50 mm Hg; pCO2 70 mm Hg; bicarbonate 45 mmol/l.

Now, normally, we would expect that chronic obstructive airways disease would produce a rise in HCO3 of about 4 mmol/l for every 10 mm Hg pCO2 rise, i.e. in this case 12 mmol/l HCO3 rise to a final level of 37, not 45 mmol/l. Normally, also, in a chronic compensated respiratory acidosis from COPD, we would expect the pH to fall by approx. .02 units for every 10 mm Hg rise in pCO2, so that the pH should be about 7.34 if we are dealing with COPD alone. The only way we could account for the greater elevation of bicarbonate and pH when calculated from pCO2 would be by a super-imposed metabolic alkalosis. Accordingly, it would be worth checking the serum potassium level, and enquiring about previous diuretic administration.

Comment

These guidelines of blood gases in various states of respiratory and metabolic disturbances of acid base are important, but it must be emphasised that to interpret any situation you have to have a clear understanding of the **clinical context** in which the changes arose.

The most important guideline, viz.

In acute respiratory acidosis, plasma pH falls by approx 0.07 units for every 10mm Hg rise in arterial pCO2.

M.C.Q. QUESTIONS

A. Mechanisms in Disease

1. You are asked to see a patient with a diagnosis of acute functional hyperventilation. Which of the following would be consistent with this:

1. Arterial pO2 110 mm Hg.

2. Arterial pCO2 55 mm Hg.

3. Plasma bicarbonate 29 mmol/l.

4. Arterial pH 7.36

5. An anion gap of 22 mmol/l.

2. A 23 year old woman is admitted to the accident and emergency department of the hospital with a 2 day history of increasing "pins and needles" in the lower legs, and increasing generalised weakness and shortness of breath. Which of the following would be more in favour of hypoventilation from respiratory muscle paralysis than anxiety hyperventilation?

1. Arterial pO2 55 mm Hg.

2. Arterial pCO2 60 mm Hg.

3. Arterial pH 7.3.

4. Plasma bicarbonate 29 mmol/l.

B. Problem-Solving

Problem 1. **(No graphic solution)**

1. A 62 year old woman (1) is brought into the emergency room (2). She is very confused and unable to give any satisfactory history (3). Examination reveals a semi-comatose patient mumbling incoherently (4). No specific localising CNS signs (5). Hands and feet cool (6) but normal colour (7). Skin rather dry (8). Pulse normal (9). JVP 1cm. above the manubrio-sternal angle (10). BP 140/80 mm Hg (11). Heart NAD (12). Chest NAD (13). Abdomen NAD (14). Temperature normal (15). Respiration rate 30/min and deep (16). Urine NAD; no glucose, ketones negative (17).

Investigations: Arterial blood analysis: plasma Na+ 144 mmol/l (18); K+ 3.0 mmol/l (19); CL- 101 mmol/l (20); HCO3- 20 mmol/l (21); pH 7.20 (22); pO2 110 mm.Hg. (23); pCO2 23 mm Hg (24); urea 4 mmol/l (normal < 7) (25); creatinine 95 micromol/l (normal 50 -100) (26); plasma glucose normal (27); plasma ketones normal (28).

Comments:

This lady clearly has an acidosis of some type. The arterial pCO2 is low so this cannot be a respiratory acidosis. It is therefore a metabolic one. The anion gap is 26 mmol/l, i.e. much greater than the upper limit of normal (20 mmol/l) so that this cannot be due to, say, the ingestion of ammonium chloride. The ketones are negative and blood and urine glucose normal, so this is not diabetic ketoacidosis. There is no clinical evidence of hypoperfusion of the periphery, nor any evidence of tenderness in the abdomen which might indicate small gut ischaemia, so this is not likely to be due to lactic acidosis (and plasma lactate turned out to be normal). As it happened, blood and urine measurements showed high levels of salicylate due to aspirin over-dosage, but a similar situation could equally have been brought about by methanol ingestion (metabolised to formic acid), paraldehyde (metabolised to acetic acid), or ethylene glycol (metabolised to oxalic acid).

Note: One of the odd things about this lady's blood picture is the relatively low plasma potassium in comparison with the degree of acidosis; also the relatively high plasma bicarbonate. This turned out to be due to the fact that she had been on thiazide diuretics beforehand, causing chronic metabolic alkalosis. This may have protected her to some degree against this acute metabolic acidosis, i.e. prevented the pH from falling to even lower levels. Knowledge of this would have been important, for two reasons:

First, because of the diuretics, there could be a prior background of ECF volume depletion which would need to be corrected. Second, sodium bicarbonate should not be given in this situation to correct the acidosis, because potassium will then rapidly go back into the cells, causing the plasma potassium to fall precipitately, with the likely induction of hypokalaemic ventricular fibrillation and death.

N.B. The induction of hypokalaemia during the correction of metabolic acidosis is such a danger that we don't usually give bicarbonate in any form of clinical metabolic acidosis (the commonest being diabetic keto-acidosis) even if the pH is less than 7.0. We now recognise that - quite apart from its adverse effect on plasma K+ - and despite its improving blood pH - it may aggravate intracellular acidosis and very much worsen the patient's overall condition. In most forms of metabolic acidosis there is an associated sodium loss, and correcting this, by say IV isotonic NaCl, allows the returning renal blood flow and function gradually to restore the blood pH to normal. Even so, you will have to stay with your patient to monitor and maintain plasma potassium very closely, because it will still tend to fall - especially in inorganic and diabetic acidosis, where intracellular K+ is very low to begin with. So much is this a hazard, particularly in diabetic keto-acidosis, that we tend to give potassium

supplements right from the outset, even when the initial plasma potassium is high! (See Ch. 17 for more detail)

Problem-Solving Case 2.

2. History: A 57 year old male builder (1) is admitted with a five day history (2) of increasing vomiting, anorexia, constipation (3) and thirst (4). He has not seen any blood in the vomitus or black "coffee-ground" material (5) but has sometimes recognised old food (6) and has also noticed that the vomitus is often projectile (7). He has noticed no shortness of breath (8), but has had weight loss of at least 3 kg over the five days (9). No shivers and sweats (10), but in the last 10 days (11) he has had a severe episode (12) of his long-standing ('years') recurrent episodic (13) "burning" epigastric pain (14) which is usually relatively mild (15), lasting on average 2-3 weeks (16) and occurring every 6-12 months (17). During each bout, the pain tends to come on about 1/2 hour after meals (18) and is relieved within 10-15 minutes by ant-acids (19). It has not woken him at night (20). Otherwise he has been reasonably well (21).

There is no relevant family history and he has not been on any drugs, in particular no diuretics (22). Occas. alcohol only. Normally smokes 20 cigarettes per day, more over the past month (23) of business related stress (24).

On examination: A thin man (25) with lax dry skin, poor tissue turgor - as judged over the forehead and cheekbones - (26). Dry tongue (27). Hands rather cool (28), pulse 115/min (29), BP 120/60 (30); 100/50 standing (pulse 130/min) (31), JVP difficult to see even with the patient lying flat, but pressure above the clavicle shows that it does fill slowly (32). Heart NAD, chest NAD (33), peripheral pulses all weak but palpable (34). Temperature 36.5 deg. C. (35). Abdomen distended, particularly in the left upper quadrant (36), where a succussion splash noted (the patient has not had anything to drink or eat for the last four hours at least) (37), and visible peristalsis (38). No suprapubic percussion dullness (39). PR: NAD except for small amount of hard faeces (40); no blood or melaena (41). Nursing chart urine testing: Urine dark, S.G.= 1.025 (42); no bilirubin, trace urobilinogen (43); no glucose (44); ketones ++ (45); urine acid (pH on dipstick = 5.5) (46).

Arterial blood shows the following results: pH 7.64 (47); HCO_3^- 36 mmol/l (48); pCO_2 48 mm Hg (49); pO_2 72 mm Hg (50); plasma Na^+ 130 mmol/l (51); K^+ 2.2 mmol/l (52); CL^- 86 mmol/l (53). Urinary sodium 5 mmol/l (54); urinary K 15 mmol/l (55); urine volume 400 ml per 24 hours (56); plasma creatinine twice normal (57); blood urea 6 times normal (58).

Graphic solution now available, but try to solve the problem with the four column method and answer the questions before viewing. You will get more from it that way, and no-one will ever know how many made 'foolish' mistakes you may have made.

Which of the following statements about this patient is/are correct?

1. This patient has evidence of depletion of the extra-cellular fluid volume.

2. There is evidence of a metabolic alkalosis.

3. The pain is suggestive of recurrent pancreatitis.

4. Anatomically, the lesion underlying the problem is most likely at a high gastro-intestinal level.

5. The nursing staff have almost certainly made a mistake in recording this man's urinary pH.

6. The hypokalaemia is fully explained by loss of potassium in the vomitus.

7. Plasma renin is likely to be suppressed.

8. The arterial blood gases suggest that this man has underlying chronic obstructive airways disease.

9. The high urea out of proportion to the elevation of plasma creatinine is compatible with an element of pre-renal impairment.

10. Metabolic alkalosis could be a contributing factor to this man's high blood urea.

Answers at end of chapter.

PROBLEM SOLUTION: CASE 2:-1

Ch. 15. Acid/base problem.

Where?	What?	How?	Why?
High G-I Obstn. + Ulceration @ Gastric outflow tract = **Pyloric**	2. 5 days = **Acute** 3, 7. Increasing = **Progressive Process ?obstruction** 10. No fever = Unlikely inflam. 11, 12. 10 days = **Severe acute episode** 13 – 17. Years = Chronic remitting & relapsing process 14-19. **? Ulcerative process** **Obstruction/ Ulceration**	3. Vomiting. ? 1° or 2° Anorexia, constipation. ?2° to vomiting. ? Upper G-I obstruction. 4. Thirst ? 2° to water/ECF depletion. from 3. 5. No haematemesis 6. Old food = Slow gastric transit time 7. Projective vomiting = **? High G-I obstruction** 8. No SOB. 9. 3 Kg. Wt. loss = ? Fluid depln. sec. to vomiting 14. Episodic 'Burning' epigastric pain, 18, Occurring after meals, 19. Relieved by 'antacids' = **? Gastric origin** 20. No nocturnal pain – time of highest acid secretion. Therefore: less likely to be duodenal ulcer – (Duod. more sensitive to acid) 21. Well otherwise	1. Male, - builder, - aet. 67 22. F.H. negative No Mx. 23. Occas. EtOH **Cigs**: 20/day 24. Business **Stress**
Interim conclusions 1.			
? Pylorus	**Acute on Chronic Ulceration Fibrosis, Oedema & Obstruction**	**Fluid depletion Sec. to gastric obstruction**	**Bkgd. Cigs & Stress**

PROBLEM SOLVING-2:-2

Examination findings

Where?	What?	How?	Why?
	25. Thin = Sec. to recent weight loss.	26. Poor tissue turgor 27. Tongue dry = Dehydration/ECF volume depletion 28. Hands cool = Poor peripheral perfusion. 29. Pulse 115/min. = Increased pulse rate 30. B.P. 120/60 = B.P. relatively low. 31. B.P 100/50 standing = Significant postural B.P drop. Pulse increase on standing = Normal baroceptor response = No vascular autonomic defect 32. JVP low = Reduced vascular volume 26-32. = **Reduced ECF volume**	
	35. Temp normal = No generalized inflammation.	33-34. CVS. and Resp. systems otherwise normal 36. Distended L. upper abdo = ? gastric dilatation 37. Gastric dilatation 38 Visible gastric peristalsis =	
37 & 38. = **Pylorus**	37. & 38. ⇔ **Obstruction**	37. & 38. = **Gastric outflow obstruction**	
	? obstruction sec. to chronic inflammation/ recurrent ulceration	39. No supra-pubic dullness = No enlarger baldder. 40. Rectal exam: hard faeces = constipation Sec. to both gastric obstruction & fluid depletion	
	41. No P.R. blood or melaena = No active gastric bleeding = **No active gastric ulceration**	41. No rectal blood or melaena = ⇔ **No active G-I/ gastric bleeding** 42. Urine: S.G. 1025 = Concentrated urine = Sec. to fluid (water) loss 43. No bilirubin or urobilinogen 44. No glycosuria = Not diabetic. 45. Ketonuria = Prob. Sec to poor calorie (fat) intake. 46. Acid urine: Odd , given acid loss from stomach with vomiting. = **Paradoxical aciduria**	

Interim conclusions 2.

? Pylorus	**Acute on chronic pyloric fibrosis from recurrent ulceration**	**Pyloric obstruction** with vomiting & **Secondary fluid depletion**	**Bkgd. Stress**

PROBLEM SOLVING 2:-3

Investigations:

Where?	What?	How?	Why?
	? COPD	47. Arterial pH 7.64 = Alkalosis expected with vomiting of acid. 48. High bicarbonate = Sec. to partial respiratory compensation for metabolic alkalosis. 49. pCO2 sl. High = sec to partial Resp compensation of metabolic alkalosis 50. Low pO2 ? Sec to COPD from cigarette smoking ⇔ 51. Low plasma Na+ reflects Relatively more Na+ loss than H20 52. Plasma K+ low = Sec. to vomiting. 53. Cl low in keeping with low Na+ 54. Low urinary Na+ = reflects **Na+ depletion** 55. Somewhat high Urine K+ Odd in context of low plasma K+ = Sec. to avid K+ exchange for Na+ in DCT in context of Na+ depletion. 56. Urine vol. of 400 ml reflects min obligatory urine vol in context of ECF vol. Depletion 57. Plasma Creatinine raised = **Reduced GFR** Secondary to ECF vol. Depletion 58. Urea raised more than creatinine = Sec. to ECF vol. Depletion. (Urea clearance lessens with low urine flow rates)	**Cigarettes**
Interim conclusions. 3.			
1. Pylorus.	**Acute on chronic recurrent ulceration. Sec. oedema & scarring**	**Pyloric obstruction** with sec. vomiting, **ECF vol. depletion, low K+ and alkalosis** with **paradoxic aciduria**.	**Bkgd. Stress**
2. Lung	**? COPD**	**Low arterial pO2**	**Cigarette smoking**

PROBLEM SOLVING 2:-4

Conclusions: Final Diagnosis

1. **Pylorus**.	**Acute on Chronic Recurrent ulceration with Sec. oedema and scarring**	**Pyloric obstruction** with sec. vomiting, **ECF vol. depletion**, **low K+** and **alkalosis** with some attempt at respiratory compensation, but limited by **paradoxic aciduria** (low availability of K+ in renal DCT limits K+ exchange for Na+ in context of avid drive for Na+ reabsorption from Na+ depletion. H+ ion takes over role of K+)	**Bkgd. Stress**
2. **Lung**	**? COPD**	**Low arterial pO2**	**Cigarette smoking**

MCQ ANSWERS

A. Mechanisms in Disease.
1 only correct.

B. Problem Solving Case 2.
1, 2, 4, 5, 8, 9, 10 correct. all others false.

Re 5: K+ is lost in vomitus, but there is also a component of inappropriate urine K+ excretion in the distal convoluted tubule inmexchange for avid Na+ reabsorption in the context of Na+ depletion.