normal anion gap acidoses [created by Paul Young 15/12/07]

general

- In hyperchloraemic acidosis, the anion-gap is normal (in most cases). The anion that replaces the titrated bicarbonate is chloride and because this is accounted for in the anion gap formula, the anion gap is normal.
- if hyponatraemia is present the plasma [Cl-] may be normal despite the presence of a normal anion gap acidosis. This could be considered a 'relative hyperchloraemia'.

reasons why high AG acidoses may give a normal AG

1. One possibility is the increase in anions may be too low to push the anion gap out of the reference range.
- In lactic acidosis, the clinical disorder can be severe but the lactate may not be grossly high (eg lactate of 6mmol/l) and the change in the anion gap may still leave it in the reference range. So the causes of high anion gap acidosis should be considered in patients with hyperchloraemic acidosis if the cause of the acidosis is otherwise not apparent. Administration of IV saline solution may replace lost acid anion with chloride so that treatment may result in the acidosis converting to a hyperchloraemic type.

2. Another possibility is intracellular movement of acid anions in exchange for chloride
- In lactic acidosis, the movement of lactate intracellularly in exchange for chloride occurs via an antiport. It has been found that when lactic acidosis occurs in association with grand mal seizures then as many as 30% of this group of patients may present with a hyperchloraemic component to their acidosis.

3. The situation may also be due to the wide normal range of the anion gap.
- This could result in a situation where the anion gap is only elevated slightly or still within the normal range due to the combination of small errors in the measurement of the component electrolytes.

major causes

Causes
- the predominant mechanism is loss of base (bicarbonate or bicarbonate precursors) and this may occur by either GIT or renal mechanisms.
- A gain of acid can occur with certain infusions but this situation can be diagnosed easily on history.

other causes

(i) Recovery Phase of Diabetic Ketoacidosis
- Hyperchloraemic metabolic acidosis commonly develops during therapy of diabetic ketoacidosis.

(ii) Chronic Administration of Carbonic Anhydrase Inhibitors
- Normally 85% of filtered bicarbonate is reabsorbed in the proximal tubule and the remaining 15% is reabsorbed in the rest of the tubule. In patients receiving acetazolamide (or other carbonic anhydrase inhibitors), proximal reabsorption of bicarbonate is decreased and distal delivery is increased. The distal tubule has only a limited capacity to reabsorb bicarbonate and when exceeded bicarbonate appears in the urine. This results in a hyperchloraemic metabolic acidosis. This can be considered as essentially a form of proximal renal tubular acidosis but is usually not classified as such.

(iii) Oral Ingestion of Acidifying Salts
- Oral administration of CaCl2 or NH4Cl is equivalent to giving an acid load. Both of these salts are used in acid loading tests for the diagnosis of renal tubular acidosis. CaCl2 reacts with bicarbonate in the small bowel resulting in the production of insoluble CaCO3 and H+.The hepatic metabolism of NH4+ to urea results in an equivalent production of H +.

renal loss of HCO3

Comparison of Major Types of RTA

	Type 1	Type 2	Type 4
Hyperchloraemic acidosis	Yes	Yes	Yes
Minimum Urine pH	>5.5	<5.5 (but usually >5.5 before the acidosis becomes established)	<5.5
Plasma potassium	Low-normal	Low-normal	high
Renal stones	Yes	No	No
Defect	Reduced H^+ excretion in distal tubule	Impaired HCO_3 reabsorption in proximal tubule	Impaired cation exchange in distal tubule

GIT bicarbonate loss

General
- Secretions into the large and small bowel are mostly alkaline with a bicarbonate level higher than that in plasma. Excessive loss of these fluids can result in a normal anion gap metabolic acidosis.
- Some typical at risk clinical situations are:
(i) severe diarrhoea
(ii) villous adenoma
(iii) external drainage of pancreatic or biliary secretions (eg fistulas)
(iv) chronic laxative abuse
(v) administration of acidifying salts

Severe diarrhoea
- This can cause either a metabolic acidosis or a metabolic alkalosis. Development of a significant acid-base disturbance requires a significant increase in stool water loss above its normal value of 100 to 200 mls/day. The more fluid and anions lost, the more marked the problem.
- Hyperchloraemic metabolic acidosis tends to be associated with acute infective diarrhoea. This is the classical finding in patients with cholera. The problem is an excessive loss of bicarbonate in the diarrhoeal fluid.
- Diarrhoeas which are caused by predominantly colonic pathology may cause a metabolic alkalosis: this includes chronic diarrhoeas due to ulcerative colitis, colonic Crohn's disease and chronic laxative abuse.

Multiple Factors which affect Acid-Base balance in patients with Severe Diarrhoea

Situation	Comment
Acute infective diarrhoea (small bowel origin)	Normal anion gap(hyperchloraemic) metabolic acidosis due loss of bicarbonate
Chronic colonic diarrhoea	May be metabolic alkalosis due predominant loss of Cl-
Hypovolaemia causing prerenal renal failure	High anion gap acidosis due to renal retention of phosphate &sulphate.
Hypovolaemia causing peripheral circulatory failure	Type A lactic acidosis
Hypovolaemia causing an increase in plasma protein concentration (increased unmeasured anion)	Increased anion gap
Vomiting	Metabolic alkalosis due loss of gastric HCl
Abdominal pain	Hyperventilation (respiratory alkalosis)

Villous adenoma
- This can cause hypokalaemia. Acid-base disorders may also occur: this is:
(i) a hyperchloraemic acidosis if bicarbonate is the principal anion lost, or:
(ii) a metabolic alkalosis if chloride is the predominant anion lost.

Drainage of pancreatic or biliary secretions
- Loss of these secretions can cause a hyperchloraemic acidosis due to the high bicarbonate levels in these secretions. The frequency and severity depend on the daily volume of secretions lost. Low output fistulae don't cause a problem.
- Pharmacological treatments (eg somatostatin) which decrease the volume lost by high output fistulae are effective at preventing the acidosis.

Losses via a nasogastric tube
- In patients with a small bowel obstruction, these losses can be predominantly of bile and pancreatic secretions and cause an acidosis (rather than an alkalosis as is usual with severe vomiting). Patients on proton pump inhibitors or H2-blockers may also be more likely to lose predominantly alkaline secretions.

Urinary Diversions
- Implantation of the ureters into the sigmoid colon or a vesicocolic fistula can result in a hyperchloraemic acidosis due to absorption of Cl- in exchange for HCO3- across the bowel mucosa.
- Absorption of urinary NH 4+ in the sigmoid colon may also contribute to the development of acidosis as metabolism of the ammonium in the liver results in production of H+. Some of these patients develop renal failure related to infection, stones or urinary obstruction. This can result in uraemic acidosis or renal tubular acidosis as well.
- Acidosis is much less of a problem with an ileal conduit (acidosis incidence 2 to 20%) than it was with the older procedure of ureterosigmoidostomy (incidence 30-80%). This is because the continuous external drainage from the ileal conduit usually results in a short dwell time in the conduit with minimal time for Cl--HCO3- exchange.
- The presence of urinary diversion operations will usually be obvious from the history