- 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.
- Hyperchloremic 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.

## 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 hyponatraemia’.

### Table: Multi factors which affect Additive balance in patients with Acute Diarrhoea

<table>
<thead>
<tr>
<th>Situation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute infective diarrhoea (small bowel origin)</td>
<td>Normal anion gap (hypochloremic) metabolic acidosis due to loss of bicarbonate</td>
</tr>
<tr>
<td>Chronic diarrhoea</td>
<td>May be metabolic alkalosis due to predominant loss of Cl⁻</td>
</tr>
<tr>
<td>Hypokalaemia causing renal failure</td>
<td>High urinary excretion of phosphate and potassium</td>
</tr>
<tr>
<td>Hypokalaemia causing peripheral dialysate failure</td>
<td>Type A Acidosis</td>
</tr>
<tr>
<td>Hyperkalaemia causing an increase in plasma protein concentration (decreased unmeasured anion)</td>
<td>Increased anion gap</td>
</tr>
</tbody>
</table>

Drainage of pancreatic or biliary secretions
- Loss of these secretions can cause a hyperchloremic 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.

## 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.
2. Another possibility is intracellular movement of acid anions in exchange for chloride so that treatment may result in the acidosis converting to a hyperchloraemic type.
3. The situation may also be due to the wide normal range of the anion gap.

## 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.

## Major Causes

1. Recovery Phase of Diabetic Ketoacidosis
2. Chronic Administration of Carbonic Anhydrase Inhibitors
3. Oral Ingestion of Acidifying Salts

## 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 hyperchloremic metabolic acidosis. This can be considered as essentially a form of proximal renal tubular acidosis but is usually not classified as such.

## Oral administration of CaCl2 or NaHCO3 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+. 

### Table: Comparison of Major Types of Acidosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden onset</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Normal pH pre-&lt;5.5</td>
<td>&lt;5.5 (usually &lt;5.0)</td>
<td>&lt;5.5 (usually &lt;5.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine pH</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Renal Stones</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Acidosis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### Urinary Diversions
- Implantation of the ureters into the sigmoid colon or a vesicocolic fistula can result in a hyperchloremic acidosis due to absorption of Cl⁻ in exchange for HCO3⁻ across the bowel mucosa.
- Implantation of urinary NH4⁺ 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 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.