THE NORTHERN HOSPITAL

HYPOKALEMIA

Remains of the massive 16th Century Tudor Warship, "The Mary Rose", Portsmouth, UK

One of England's worst naval disasters occurred on 19 July 1545. As Henry VIII's greatest warship, the Mary Rose was sailing out from Portsmouth to engage the French, it was seen to inexplicably lean alarmingly to one side, then capsize and sink. Only about 40 men out of a crew of around 700 survived. On 11 October 1982 an incredible engineering feat allowed the wreck to be raised from the seabed where it had laid for 437 years.

The wreck is one of the most important maritime archeological finds ever. It is the only 16th century warship ever recovered anywhere in the world and now resides at the Portsmouth Maritime Museum. It provides a priceless time capsule of the mid 16th century with over 20,000 artifacts, including human remains recovered along with the wreck. It has given historians and archaeologists great insight into the construction and workings of 16th century warships. She was one of the first ships equipped with cannons that could fire broadside and technologically is seen

as a transition ship that marks the evolution from the old medieval floating castles to the galleons of Elizabeth I's navy.

One of the greatest mysteries of the Mary Rose is why it actually sank. Current expert opinion believe it was a combination of factors, including the fact it was carrying 700 men at the time, though only designed to carry around 400. Further it is thought that several refits were made to accommodate many more guns than its original design. As it was making a tight turn in preparation to fire on an enemy ship the extra weight together with a freak gust of wind caused the ship to tilt. Already low in the water due to this added weight the final straw seems to have been an oversight of the crew - a failure to close the lower gunports, which rapidly took in water, thus causing the Mary Rose to sink beneath the waves.

In hypokalemia, it is important to recognize the alarming tilt of the starboard U wave rising up over the rapidly sinking port side T wave. Treatment must be quickly initiated to "close the gun ports", by giving potassium, lest the ST segments further sink beneath the waves with ultimately disastrous consequences.

A poignant artifact - one of the many sets Rosary Beads found in the wreck of the Mary Rose - many Sixteenth century sailors praying for Mary's protection, carried these with them into battle.

HYPOKALEMIA

Introduction

Hypokalemia is defined as a potassium level less than 3.5 mmol / L

The normal level of potassium is (around) **3.5 - 5.0 mmol / L**

In general terms the severity of hypokalemia can be defined thus:

Low normal:	3.5 - 4.0 mmol / L.
Mild hypokalemia:	3.0 - 3.5 mmol / L
Moderate hypokalemia:	2.5 - 3.0 mmol / L.
Severe hypokalemia:	Less than 2.5 mmol / L.

The most important complication will be tachyarrhythmias

Treatment consists of potassium replacement and correction of the underlying cause.

History

The brilliant English chemist **Sir Humphry Davy** (1778 - 1829) is credited with the discovery of the element potassium.

In 1807 he isolated the pure element by using a process of electrolysis. He named the new element, potassium, which he derived from the word potash.

The word potassium is derived from the old English word "potash" which referred to a traditional method of extracting potassium salts from plant material. The **ashes** of burnt plant material were heated with water in a **pot**. The water was then allowed to evaporate off, which would leave behind the "pot ash" , which was rich in potassium.

The elemental symbol for potassium is "**K**" which is derived from "kali", from the root word alkali, which in turn is derived from the Arabic word for "plant ashes", **al-qalyah.**

Physiology

The daily potassium requirements for a healthy subject is 0.5 - 1.0 mmol/kg/day.

Only about 2 % of total body potassium is extracellular, the rest is intracellular.

Pathophysiology

With normal acid - base status, a **decrease** of **1 mmol/L** in serum concentration represents a whole body potassium deficit of at least **200 mmol**.

The deficit is greater if there is associated metabolic acidosis and less if there is metabolic alkalosis.

Causes

1. Reduced intake:
    - Starvation.
    - Eating disorders
2. Increased losses:
    - GIT:
        - ♥ Vomiting and diarrhea (of any cause).
    - Renal causes:
        - ♥ Diuretic phase of ARF
        - ♥ Intrinsic renal diseases:
            - ♥♥ RTA
        - ♥ DKA:

          There will be decreased total body levels, however, this will not become apparent until treatment begins.
    - Drugs:
        - ♥ Diuretics
    - Endocrine:
        - ♥ Primary hyperaldosteronism:
            - ♥♥ Conns
            - ♥♥ Cushings
        - ♥ Secondary hyperaldosteronism:
            - ♥♥ Liver disease / nephrotic syndrome / heart failure.
        - ♥ Pheochromocytoma (high adrenaline levels)
3. Redistribution:

- Acute alkalosis (of any cause)
- Drugs:
    - ♥ **Insulin overdose**
    - ♥ B_2 agonists including adrenaline and especially IV salbutamol:
        - ♥♥ Beta adrenergic sympathomimetic agents in general:

          These can induce **hypokalemia,** via an action on beta 2 receptors that stimulate membrane sodium/potassium ATPase activity.
    - ♥ Theophylline overdose
- Periodic hypokalemic paralysis:
    - ♥ This condition is a transcellular maldistribution, not a true deficit.

4. Uncertain mechanism:

- Magnesium deficiency:

  Magnesium deficiency, by a complex series of interactions, is often seen in association with deficiencies of **potassium** and **calcium** as a "**triad of deficiency**"

  Hypomagnesemia may be a cause of refractory hypokalemia.

  The hypokalemia is induced by a mechanism not clearly understood but involving increased urinary potassium loss.

  Additionally most of the conditions that cause hypomagnesemia also cause hypokalemia, so the two should be always considered together.

Clinical Features

In most cases hypokalemia is **asymptomatic** until it becomes **severe**.

Symptoms that can occur in more severe cases include:

1. Arrhythmias:

- Ectopics, (atrial or ventricular)
- Tachyarrhythmias
- Increased QT segment (with potential for torsade).

- VT / VF

Digoxin can Enhance the cardiotoxic effects of hypokalemia.

2. Muscle weakness, (especially with hypokalemic periodic paralysis).

3. GIT disturbances, including ileus.

4. Renal tubular dysfunction:

   - Nephrogenic diabetes insipidus (with consequent polyuria and polydipsia).
   - Increased H+ ion excretion in urine resulting in alkalosis.

The combination of **hypertension** and **hypokalaemia** may represent an endocrine cause such as **hyperaldosteronism** or **pheochromocytoma.**

Investigations

Blood tests:

1. FBE

2. U&Es / glucose:

   In general terms the severity of hypokalemia can be defined thus:

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4. Magnesium/ phosphate / calcium levels.

5. ABG/ VBG:

   - Assess for alkalosis as a cause and/ or contributing factor

ECG Changes

The ECG changes that occur in hypokalemia are as follows:

1. Development of U waves (earliest sign).

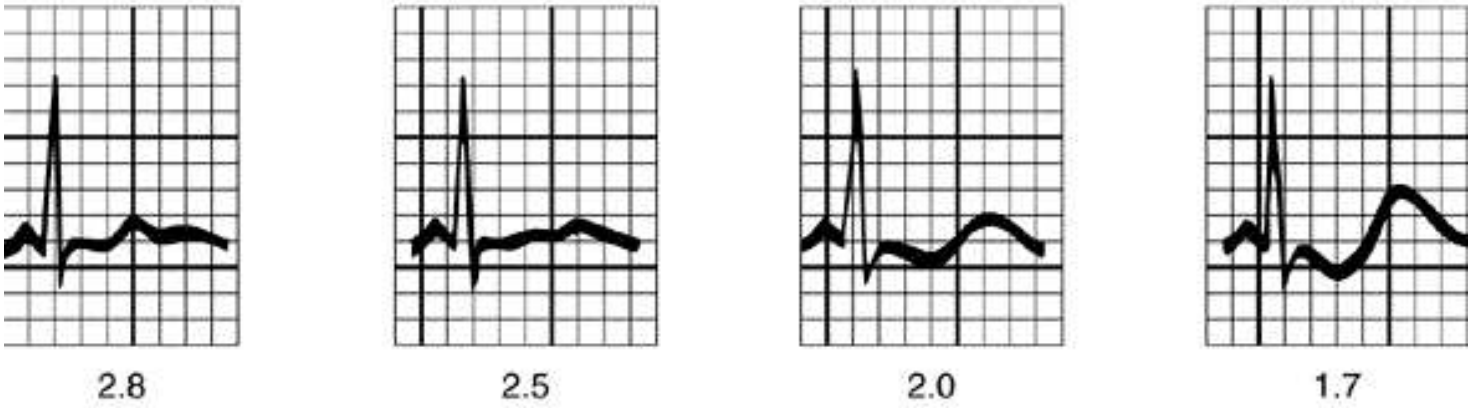
2. Depression of ST segment and flattening of T wave, with increasing prominence of U wave, (i.e as T wave flattens, the U wave increases and vice versa as hypokalemia resolves).

3. Increased QT segment (with potential for torsade).

4. Elevation of the P wave.

5. Mild prolongation of the PR interval

6. Arrhythmias, as listed above.



Series of ECG changes showing the progressive increase in the U wave in association with the progressive decrease in the T wave and development of ST depression, as the severity of the hypokalemia progresses. (Values are in mmol / L)

See also Appendix 1 below

Management

Management consists of:

1. Replacement therapy:

    - If mild, oral treatment is usually sufficient.

    - If more severe / symptomatic / unable to tolerate orally, then IV replacement will be necessary.

2. Treating the cause.

3. Replace any associated **magnesium deficiency.**

Oral treatment with Potassium chloride tablets:

1. Slow release preparations, such as **Slow K**, (8 mmol K+, or 600 mg, per tablet)

- This is generally more **palatable** and is the **preferred oral formulation**.

  The oral daily dosing range of potassium chloride sustained-release is **1200 to 3600 mg (= 16 to 48 mmol = 2-6 Slow K tablets)** orally, daily in divided doses.

2. **Chlorvescent** ("effervescent" tablets) is a liquid preparation, (14 mmol K+) with a relatively unpleasant taste.

   - It is used primarily for nasogastric tube use.

IV Replacement with Potassium Chloride:

Note that all orders for IV potassium should be given in mmols.

All patients receiving IV potassium (above routine maintenance requirements) must be on ECG monitoring.

IV Preparation:

- Potassium chloride comes in "Baxter bags" containing **10 mmols** (or **750 mgs)** of **KCl** in 100 mls normal saline.

  It is much safer to give IV potassium via these 100 ml bags than via more concentrated ampoule preparations.

  Extemporaneously adding ampoules of potassium chloride to intravenous fluids is **not safe. Inadequate mixing may result in potassium being delivered at a lethal concentration.**

  Premixed preparations are available in varying concentrations and volumes up t 1 liter.

When giving IV potassium, rapid replacement is not necessary unless:

1. There is severe hypokalaemia

2. Symptomatic hypokalaemia:

   - e.g. acute tachyarrhythmia or cardiac arrest where hypokalemia is a contributing factor.

3. The patient has an Acute Coronary Syndrome:

   - Where it is desirable to maintain potassium levels at 4-5 mmols/l

As a general rule for **IV administration:**

The rate of IV administration for mild to moderate hypokalemia is generally **5 - 20 mmols / hour.**

Rates of **20 - 40 mmol / hr** (maximum) have been used for **severe** hypokalemia **(< 2.5 mmol/L**) with the higher rates being used when there is associated **cardiac arrhythmias/ life-threatening instability.**

In these cases where higher doses are being given the following precautions should be kept in mind:

- Baseline potassium level has been documented.
- Normal renal function.
- Adequate urine output.
- ECG monitoring.

Note that rate limiting devices (such as the "IMED") should be used when giving IV potassium.

Adjunctive measures:

Hyperaldosteronism:

When hypokalaemia results from fixed mineralocorticoid excess (e.g. in primary hyperaldosteronism), restricting sodium intake is also key in achieving potassium repletion.

Vomiting:

When potassium depletion is associated with severe metabolic alkalosis (e.g. from vomiting acid stomach contents), potassium repletion may not be possible until the chloride deficit is corrected (with normal saline).

Hypomagnesemia:

Replace any associated **magnesium deficiency.**

Potassium sparing drugs:

Potassium-sparing drugs have **no place** in managing acute **hypokalaemia** but can be useful for **maintenance.**

Use:

- Spironolactone 50 to 100 mg orally, daily.

Or

Amiloride 5 mg orally, once daily, increasing to a maximum of 10 mg twice daily.

The response to continuing treatment with potassium-sparing drugs should be reviewed every 1 to 2 weeks until the serum potassium concentration is stable.

This is to avoid overcorrection of the deficit and the development of potentially dangerous hyperkalaemia.

The lowest effective dose should be used.

Monitoring:

In general terms:

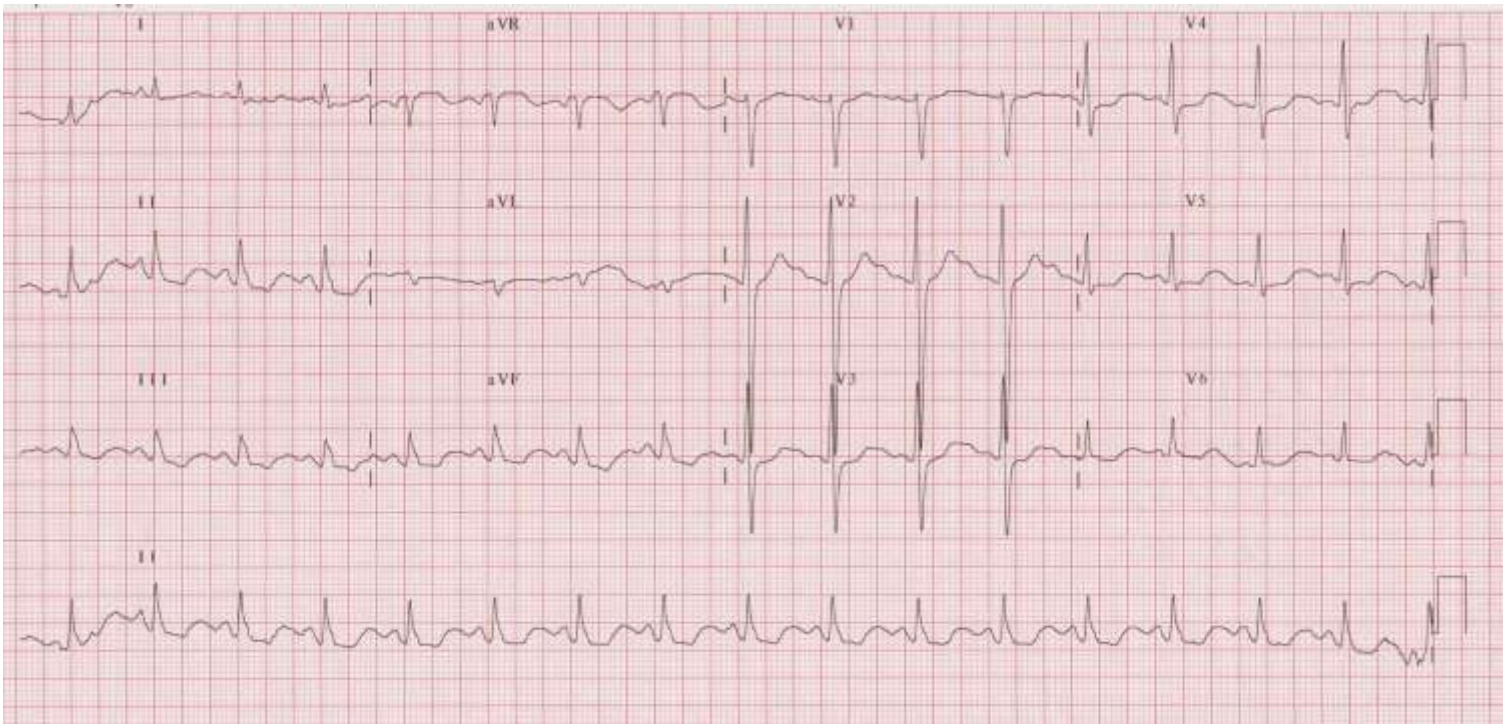
The serum potassium concentration should be measured every 2 hours.

Potassium phlebitis:

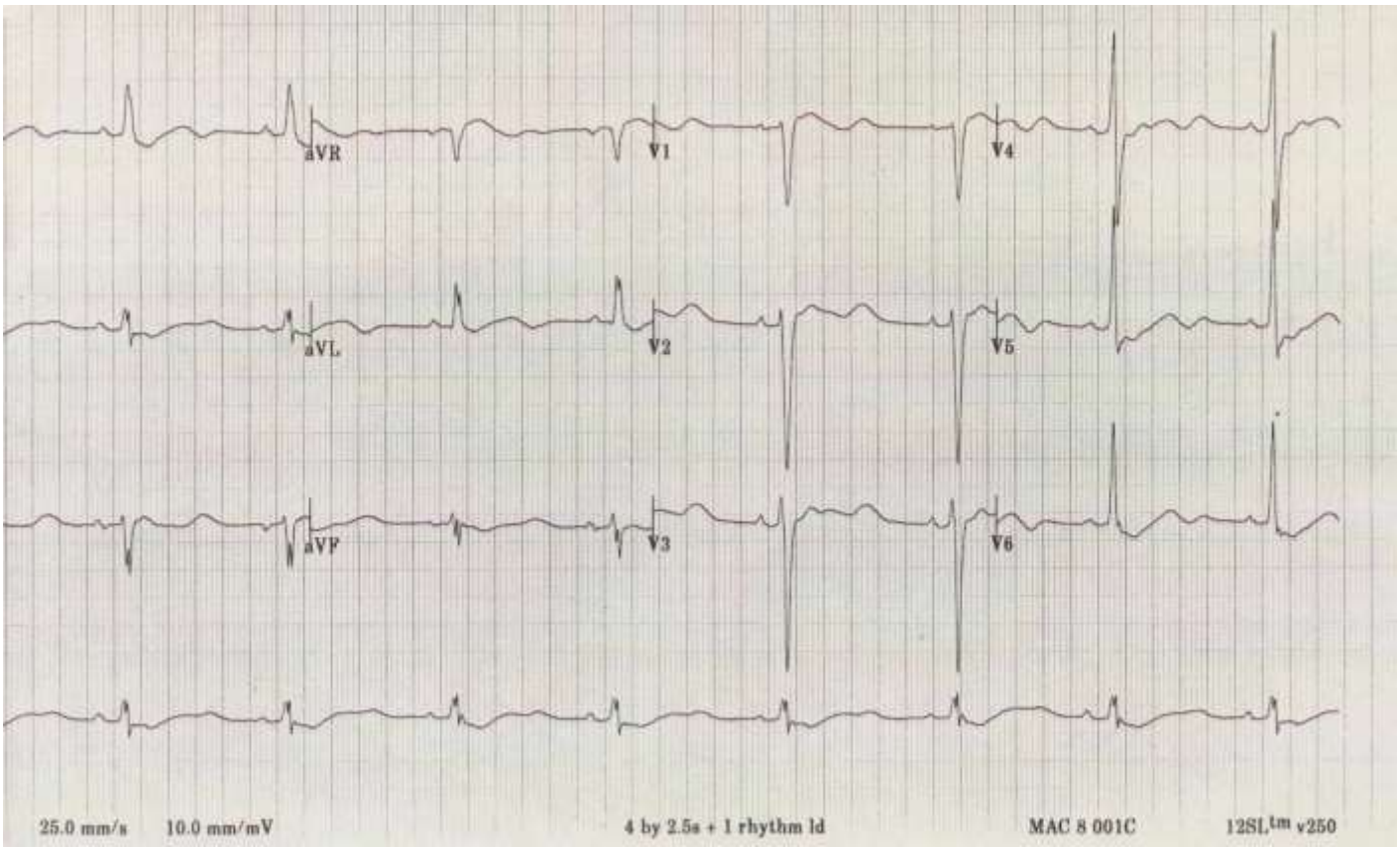
Note that IV potassium may result in painful venous phlebitis. This may be addressed by:

- Giving the potassium in dilute solutions.
- Giving the potassium into a larger peripheral vein.
- Giving the solution more slowly.
- Ensuring thorough mixing of solutions prior to administration.

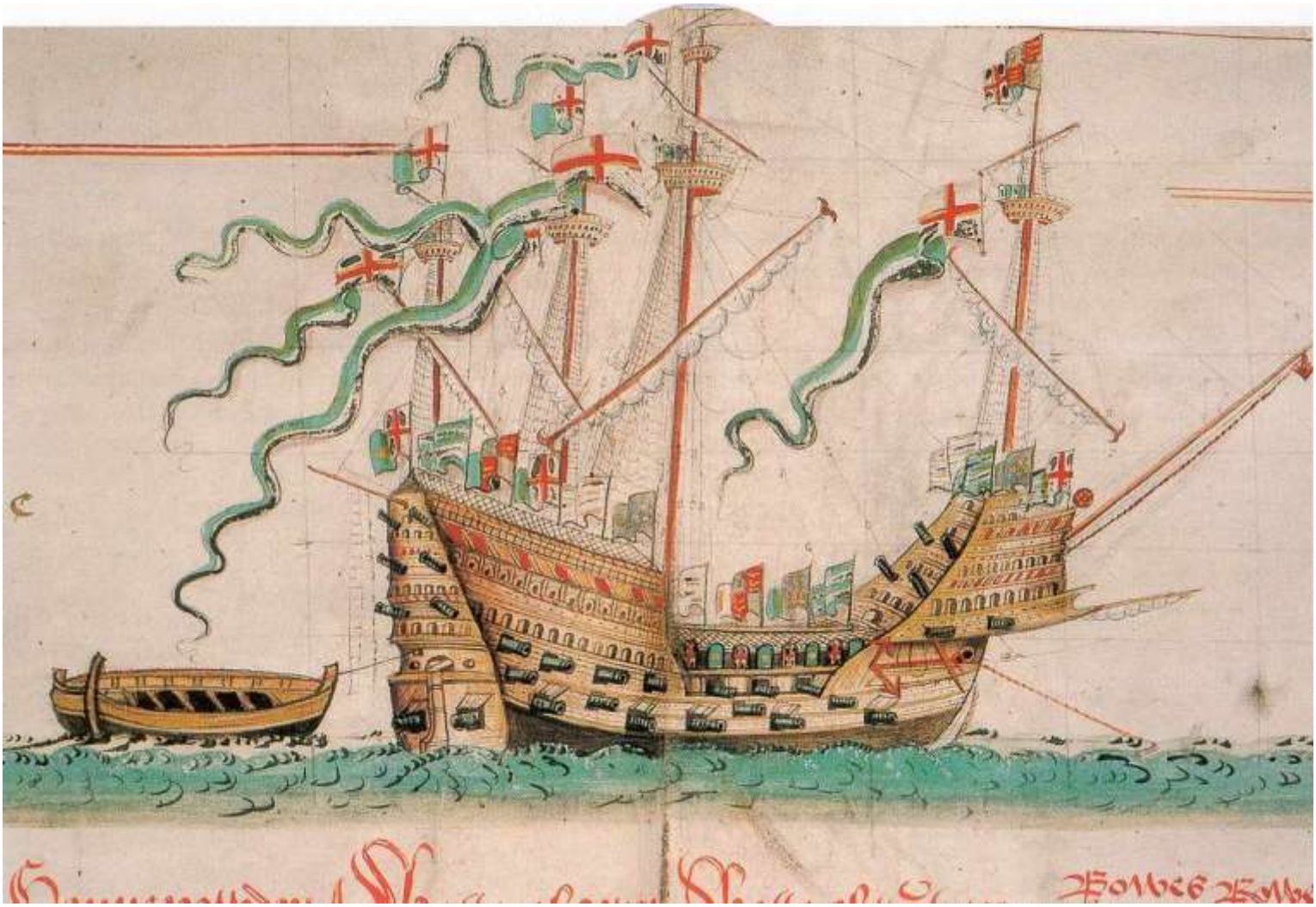
Appendix 1



12 lead ECG of a patient with RTA and moderately severe hypokalemia (potassium level of 2.6 mmol/L).



12 lead ECG of a patient with severe hypokalemia (1.4 mmol/L), (Courtesy Dr Mark Santamaria).



The Mary Rose, The Anthony Roll, 16th century

A contemporary depiction of the flagship of the Tudor Navy, "The Mary Rose". It demonstrates the typical appearance of a Sixteenth century carrack, with "castles" fore and aft.

The image comes from the Anthony Roll which is a Sixteenth century record of ships of the English Tudor navy of the 1540s. The Roll originally consisted of three rolls of vellum, depicting 58 naval vessels giving information on the size, crew, armaments, and basic equipment of each vessel. They belonged to Henry VIII who kept them in the royal library. In 1680 Charles II gave two of the rolls to Samuel Pepys, which are now in the Pepys Library at Magdalene College, Cambridge. The third roll remained in the royal collection until William IV gave it to his daughter, Mary Fox, who later sold it to the British Museum in 1858. Today resides in the British Library.

References

1. Victorian Guideline for Replacement of Potassium developed by Victorian Medication Safety Committee (VMSC), January 2005.

2. Conover M, Understanding Electrocardiograpghy 7th Ed 1996, p.276-79.

3. eTG - April 2019

4. Pasco J. Electrolyte Disturbances in Textbook of Adult Emergency Medicine, Cameron et al Churchill Livingstone 4th ed 2015.

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