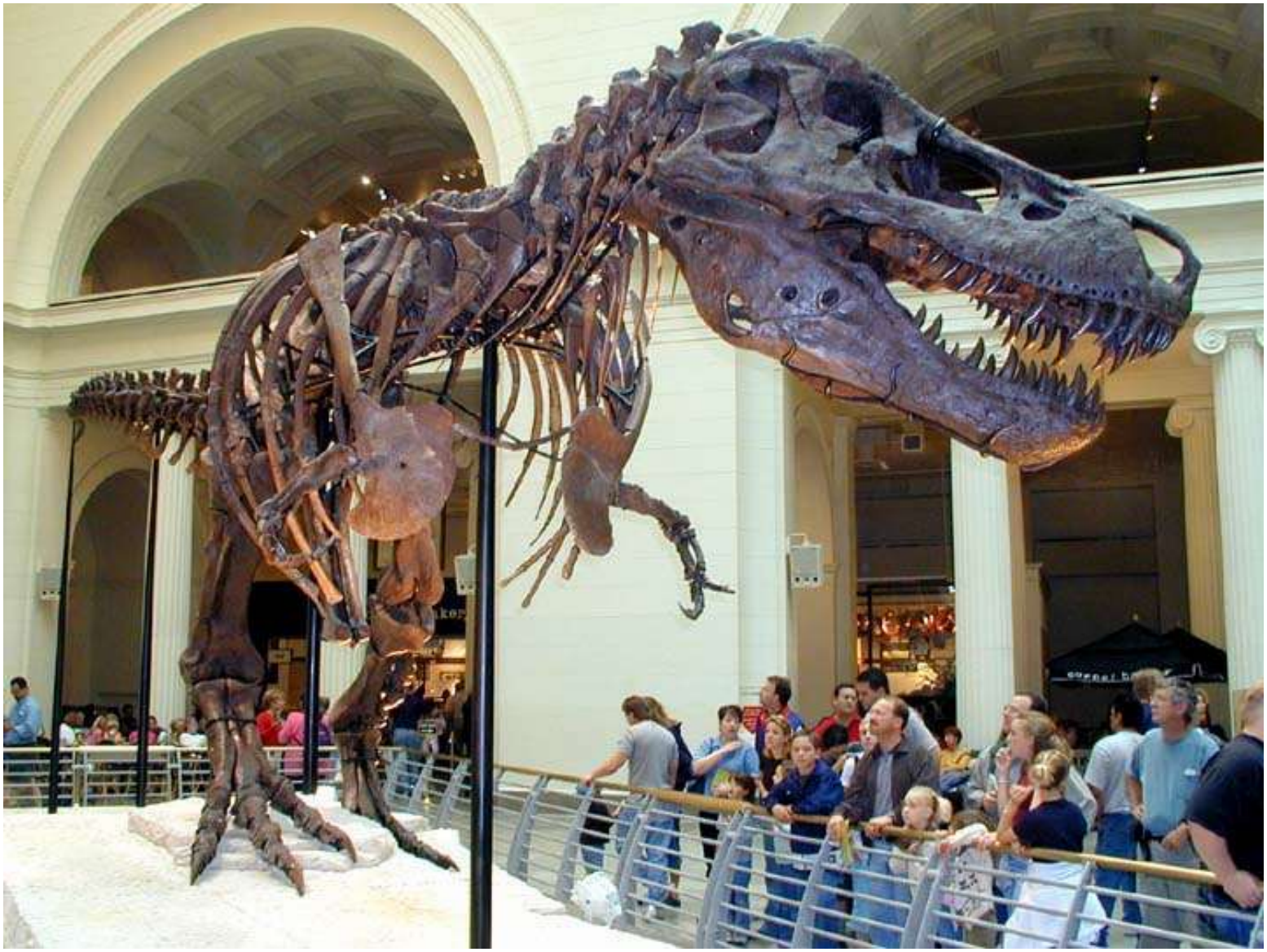
THE NORTHERN HOSPITAL

HYPERKALEMIA



"Sue", fossilized skeleton, Tyrannosaurus Rex, Late Cretaceous Period, 67 million years old, Field Museum Chicago Illinois.

It is not yet clear what role volcanism will play in our final understanding of catastrophic events on Earth. But as the list of known impact craters increases by two or three a year, and as impact debris is found in more and more places in the rock record, the impact of comets and asteroids is being accepted by more and more geologists as a normal process on Earth., as it obviously is elsewhere in the Solar System. The Yucatan impact was unusual because of its magnitude, which was sufficient to cause a mass extinction, but it is simply one of the larger events in a continuum of impact magnitudes. Objects of all sizes fall to Earth, and the smaller

ones fall much more frequently. The smallest objects, of sand grain size and smaller, do not hit the Earth's surface because they burn up by friction high in the atmosphere, making the streaks of light we call meteors. Meteors are so frequent that almost anyone who lives away from bright lights can see one every few minutes in the dark night sky.

One would think that the only collisions visible in the sky would be the streaks of light from micrometeorites. But, unexpectedly, the dramatic event that fully confirmed the end of uniformitarian geology was not seen by looking down at the rocks which record Earth history, but by looking upward.

More than any other single person, Gene Shoemaker has been the central figure in the growing understanding of impact craters, in the expansion of geology throughout the Solar System and in the laying to rest of Nineteenth century uniformitarian dogma. From his early days of studying the Moon through a small telescope and dreaming of going there, to his proof that Meteor Crater is an impact scar, to his training of the astronauts for lunar missions, to his scientific leadership of one deep-space probe after another, to his discoveries about the KT boundary impact, to his many expeditions to study impact craters in the Australian desert - Gene has always been at the forefront.

It is thus appropriate indeed that the final episode in this telling of the impact - extinction story should center on Gene Shoemaker, his wife Carolyn and their friend David Levy. For years Gene and Carolyn often with David would journey to the astronomical observatory on Palomar Mountain every month in the dark of the Moon, were they were systematically photographing the sky again and again, gradually building up a census of Earth crossing asteroids - space rocks whose orbits can come inside the orbit of the Earth, and which thus have a chance of hitting our planet. Gene wanted to know how many of these potential threats there are, how often on the average they hit the Earth, and whether there is any immediate danger for which we should be preparing.

Carolyn has the best eye for spotting asteroids and comets on the photographic plates, so it was she who called out to Gene and David, "Look at this - I think I've got a squashed comet!" Detailed pictures soon showed that the comet they had discovered was not squashed, it was fragmented. Periodic comet Shoemaker-Levy 9, as it was designated, had been captured by Jupiter so that it orbited the giant planet, rather than the Sun. On one pass, shortly before Carolyn noticed it, the comet came too close to Jupiter, gravitational forces ripped it into fragments, and dust drifting away from the surfaces of the freshly broken fragments made the pieces of the formerly inactive comet shine in the sunlight.

The orbits of the fragments were calculated, and to the surprise and delight of astronomers and geologists, it was clear that they were going to crash into Jupiter on their next pass. Observing programs were planned in feverish haste, and as the comet fragments bore down on Jupiter in July of 1994, telescopes of all kinds, all over the Earth and out in space, were trained on the site of the impending collisions. The impacts were even more spectacular than anyone has dared hope. As the larger fragments plunged into the nearly bottomless atmosphere of Jupiter, plumes of shocked material rose thousands of kilometers above the planet and then, in Jupiter's fierce gravity, collapsed back on top of the atmosphere. Their collapse generated intense bursts of heat, which could be seen as infrared light through telescopes on Earth.

Nature was doing, at a safe distance, an experiment we could not possibly have done ourselves. Astronomers at their telescopes were awed by what they were seeing, and for those of us who had joined with Gene Shoemaker in the long fight to have impacts accepted by Earth historians, it was profoundly satisfying. It was the incontrovertible proof that big impacts are not simply a thing of the remote past. They can, and do happen right now.

The bursts of heat from the impact sites on Jupiter were intellectually satisfying, but they were also sobering and deeply moving. For as we watched the violence being inflicted on another planet, we were seeing a reenactment of the last spectacle ever witnessed by Tyrannosaurus rex - the deadly flash from the Crater of Doom, on the day the Mesozoic world ended.

Walter Alvarez, "T. Rex and the Crater of Doom", 1997.

Postscript:

Gene Shoemaker just months after the release of Walter Alvarez's book, that popularized the story of the solving of the mystery of the extinction of the dinosaurs, was killed in a car crash on the remote Tanami Track, a few hundred kilometers northwest of Alice Springs, Australia. He had been exploring impact craters in the remote outback.

Above is "Sue", discovered in South Dakota in 1990. At over 50 feet long she is the largest and most complete Tyrannosaurus rex skeleton ever discovered and currently resides in the Field Museum, Chicago, which paid 8.4 million US dollars for her in 1997. There is convincing evidence she was killed by an altercation with a fellow T. rex, whose massive tooth was found embedded in one of her ribs. One of the most intriguing puzzles of the Earth's past history was the virtually instant demise of the Dinosaurs all over the world at the same time. In one of the greatest scientific achievements of the 20th century, the Noble prize winning Louis Alvarez and his son Walter put forward the case for a massive asteroid impact as the cause. Since 1980, when the Alvarez paper came out, there has been overwhelming geological evidence come to light confirming the asteroid impact theory. The dinosaurs would have met sudden death near the impact site without any warning of the asteroid that was silently hurtling toward the Earth. Could this event ever happen again to threaten the human race? Most Astronomers say yes and now there are increasing efforts to monitor the heavens for just such an event.

Hyperkalemia, like the silent asteroid hurtling through space, represents the threat of sudden death without warning. Just as monitoring the heavens for impending disaster is essential, so too is ECG monitoring essential in all cases of significant hyperkalemia.

HYPERKALEMIA

Introduction

Hyperkalemia is a common emergency that presents to the ED.

It is usually completely asymptomatic and can rapidly kill without warning when levels are acutely raised. [1]

Hyperkalemic ECG changes may be missed, unless the condition is *specifically considered.*

The most common causes will be **renal failure** and **drugs**.

The normal value for potassium levels is **3.5 - 5.5 mmols/liter**

In *general* terms the severity of hyperkalemia can be graded as:

Mild:	**5.5 - 6.0**	Treat the cause and give resonium
Moderate:	**6.0 - 7.0**	Above and insulin / glucose (± bicarbonate)
Severe:	**> 7.0**	All of above and IV calcium chloride

See also separate document on Potassium Chloride Overdose (in Toxicology folder)

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.**

Pathophysiology

Causes

The causes of hyperkalemia include:

1. Excessive intake:

- Overdose of oral potassium supplements.
- Iatrogenic, with:
    - ♥ Excessive IV administration
    - ♥ Massive blood transfusions.

2. Failure to excrete:
    - **Renal failure (acute or chronic)**
    - **Drugs**:

      In particular:
        - ♥ Potassium sparing diuretics
        - ♥ ACE inhibitors
        - ♥ Angiotensin II antagonists (i.e. sartans)
    - Conditions of **hypo-aldosteronism**, such as Addison's disease.

3. Re-distributive:
    - Acidosis (↓ pH by 0.1 → ↑ 0.6mmol / L K^+)

      Metabolic acidosis > respiratory acidosis.
        - ♥ Including DKA, (even though total body stores are depleted).

          Interestingly, the development of hyperkalemia in patients with diabetic ketoacidosis is more due to insulin deficiency and hyperosmolality, that it is to acidemia, (*Up to Date Website*).
    - Rhabdomyolysis (**from any cause - see also separate document on Rhabdomyolysis in Renal and Electrolytes folder**).
    - Catabolic states in general
        - ♥ Sepsis
        - ♥ Multitrauma
    - Hemolysis (including transfusion of old RBCs)
    - Hyperkalemic periodic paralysis:

- ♥ This is a genetic that is caused by autosomal dominant mutations in the skeletal muscle cell sodium channel. Patients with this disorder typically develop myopathic weakness *during* hyperkalemia induced by increased potassium intake or rest after heavy exercise.

- Drugs / toxins, in particular:
  - ♥ Suxamethonium
  - ♥ Digoxin overdose / toxicity
  - ♥ Systemic effects of hydrofluoric acid burns.

4. Pseudohyperkalemia:
   - Hemolysis of blood sample.
   - Significant delays in separating RBCs from serum
   - Extreme leucocytosis/ thrombocytosis
   - Blood taken from IV drip arm, receiving fluids with supplemental potassium.

Clinical Features

1. Hyperkalemia is completely **asymptomatic**, unless **severe.**
   - Manifestations usually occur when the serum potassium concentration is ≥ 7.0 mEq/L with chronic hyperkalemia or possibly at lower levels with an acute rise in serum potassium

Symptoms include:

2. **Arrhythmias - these can kill suddenly and without any clinical warning.**

3. Muscular weakness:
   - Hyperkalemia can cause ascending muscle weakness that begins with the legs and progresses to the trunk and arms

     This can progress to flaccid paralysis, mimicking Guillain-Barré syndrome. Cranial nerve function is typically intact, and respiratory muscle weakness is rare.

     These neurological manifestations resolve with correction of the hyperkalemia.

4. Occasionally paralytic ileus.

Clinical severity:

This will depend on:

1. Level of potassium
2. Acuteness of the rise.
3. Degree of ECG changes (over and above peaked T waves).

Investigations

Blood tests:

1. U&Es:

    - If severe hyperkalemia is suspected on ECG, an **urgent** potassium level should be requested to confirm the diagnosis (by *personally contacting the laboratory*).

      An urgent potassium level can also be quickly obtained from a VBG sample.

    - Renal impairment/ failure is the most common cause of hyperkalemia.

    In general terms severity can be graded as:

Mild:	**5.5 - 6.0**	Treat the cause and give resonium
Moderate:	**6.0 - 7.0**	Above and insulin / glucose (± bicarbonate)
Severe:	**> 7.0**	All of above and IV calcium chloride

Further blood tests will depend on the specific diagnosis that is being sought.

2. Urgent digoxin level, if digoxin toxicity is suspected.
3. VBGs,/ ABGs if acidosis is suspected.

ECG:

This will be the most urgent investigation in any patient with suspected/ actual hyperkalemia.

Typical changes can make the diagnosis, even before blood test results are available.

Hyperkalemic ECG changes may be readily missed, unless the condition is *specifically thought of:*

1. Peaking of T waves (the first manifestation) (with a with a shortened QT interval)

2. Prolonged PR interval - there is a progressive lengthening

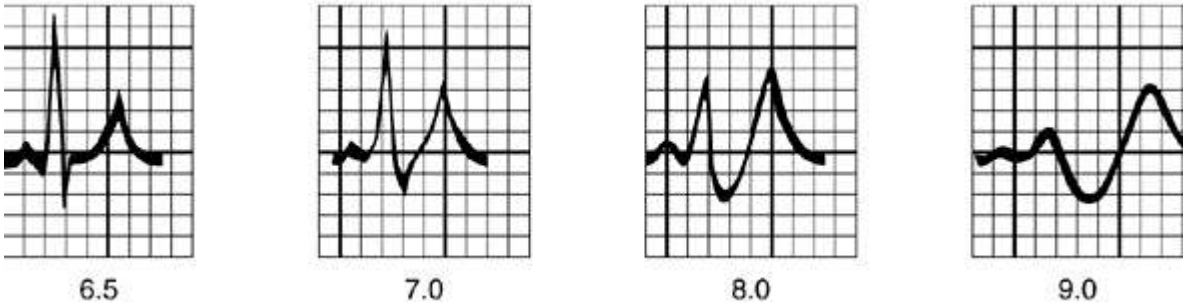
3. Flattening of P wave, which eventually disappears.

4. Widening of QRS complex, eventually merging with the T wave to form a "**sine-wave**".

5 Progressive conduction delays:

Sinus bradycardia → sinus arrest → conduction delays → slow idioventricular rhythms →asystole, (however, **VT** and **VF** may also occur).

Conduction abnormalities can include right bundle branch block, left bundle branch block, bifascicular block, trifasicular and advanced atrioventricular block.



The effects of increasing hyperkalemia on the ECG. Levels are in mmol / L.

Note however, the progression and severity of ECG changes do not always correlate well with the serum potassium concentration. The acuteness of the rise as well as the actual level is also important.

***Rapid* rises in serum potassium levels cause greater cardiac toxicity.**

Management

Severe hyperkalemia can kill without clinical warning.

Any patient found to have hyperkalemia must have an urgent 12 lead ECG followed by close ECG monitoring and early treatment as suggested by the level and the ECG findings.

Principles of Treatment

These include:

1. **Monitoring**:

   - Patients with severely elevated levels of potassium or signs of hyperkalemia on their ECGs must **remain on ECG monitoring**.

2. **Immediate protection of the myocardium**:

- IV calcium is used for immediate emergency treatment to protect the myocardium from the arrhythmia inducing effects of hyperkalemia. Calcium alleviates the membrane depolarisation effects of severe hyperkalaemia.

  This can be immediately lifesaving.

3. **Redistribute the potassium intracellularly**:

   The following are used for the intermediate term lowering of blood levels, by redistribution.

   - IV Glucose / Insulin
   - IV bicarbonate
   - Nebulized salbutamol

4. **Remove potassium**:

   - Dialysis may be used for the *rapid removal* of potassium should other measures prove unsuccessful.
   - Resonium is used for the *longer term* elimination of potassium from the body.

5. **Treat any underlying cause**

   For example:

   - Fab fragments for digoxin toxicity.
   - IV hydrocortisone for adrenal failure (but *not* insulin)

Therapeutic Agents used for Hyperkalemia

Calcium chloride/ gluconate

Indications for calcium chloride:

1. Potassium levels of > 7.0
2. ECG changes more severe than peaked T waves in isolation, (ie widening of the QRS).
3. Arrhythmias.

Give **1 ampoule calcium chloride 10mls of 10 %** (= 1 gram = 6.8 mmols of calcium) slow IV bolus, (i.e over 5-10 minutes)

Alternatively **2 ampoules of 10 % calcium gluconate** can be given as a slow IV bolus over 5-10 minutes, Note this preparation provides approximately 3 times *less* calcium than the calcium chloride preparation, (0.935 gm/10 mls = 2.2 mmols calcium) [2]

The effect is relatively short-lived and the dose may need to be repeated in **30 - 60 minutes** as required.

Calcium should not be administered as *monotherapy* for hyperkalemia but should rather be combined with therapies that also drive extracellular potassium into cells.

Calcium chloride / gluconate:

- Works within minutes
- Protects against cardiac membrane effects, i.e., arrhythmias/ conduction delays.

Glucose and insulin

- Works within 15-30 minutes. Serum potassium will decrease by 0.5-1.5 mmol/L over 30 minutes.[3]
- Redistribution of potassium (to the intracellular compartment, but does not get **rid** of it from the body).
- Give **10 U of a rapid acting (e.g. "actrapid") insulin IV** bolus *together with* **50 mls** of **50% dextrose** IV over 4 - 5 minutes.

  The administration of glucose *without insulin* is **not** recommended, since the release of endogenous insulin can be **variable** and the attained insulin levels are generally *lower* with a glucose infusion alone, (Up to Date Website).

Sodium Bicarbonate

- This is used particularly in cases **of metabolic acidosis**.
- Works within 15-30 minutes.
- Redistribution of potassium (to intracellular compartment, but again does not get **rid** of it).
- Give 1 ml/Kg of 8.4% solution (maximum 100 mls) over 5-10 minutes whilst on ECG monitor. [3]
- This may be repeated in 60 - 120 minutes. [3]

Beta2-adrenergic agonists

- Works within 30-90 minutes, (by IV or nebulized routes)

- Promotes tissue uptake of potassium into cells by an effect on Na/K ATPase.
- Give salbutamol 0.5 mg IV or salbutamol 10 - 20 mg by nebulizer

Cation exchange resins

These remove potassium from the bowel lumen, in exchange for sodium.

Give Resonium A, (sodium polystyrene sulfonate) 15 grams (suspended in 45 to 60 mL of water) orally 3 or 4 times a day.

Alternatively resonium can be given rectally, as 25 to 50 grams (suspended in 150 mL of water) as a retention enema, daily.

- Works within 1-2 hours, but may take up to 6 hours for full effect
- **Removes** potassium.

Each gram removes about 1 mmol of potassium and **delivers 2 to 3 mmol of sodium**, sodium loading can therefore be a disadvantage.

If sodium loading is problematic (renal failure) - then a calcium exchange resin me y be used instead - **Calcium polystyrene sulfonate (in 45- 60 mls of water) orally 3 - 4 times daily**, (note preparation should not be given to hypercalemic patients).

This treatment lowers the serum potassium by 0.5 to 1 mmol/L over 1 - 6 hours.

Treatment with ion exchange resin should not be continued with serum potassium <5 mmol/L, to avoid overshoot to hypokalaemia. [3]

Dialysis

Dialysis:

- Works within minutes
- **Removes** potassium.

It is used especially in cases

- **Of renal failure**
- Refractory to other medical treatment
- Of extreme / ongoing hyperkalemia as in **rhabdomyolysis** or a **potassium supplement overdose**.

Treatment according to Severity of Hyperkalemia

In general terms severity can be graded as:

Mild:	**5.5 - 6.0**	Treat the cause and give resonium
Moderate:	**6.0 - 7.0**	Above and insulin / glucose (± bicarbonate)
Severe:	**> 7.0**	All of above and IV calcium chloride/ possibly dialysis.

Severe Hyperkalemia

- **ECG monitor for all cases.**
- Give calcium, glucose / insulin / resonium / dialysis as above.

  Nebulized salbutamol is not *routinely* used due to the potential for cardiac tachyarrhythmia in an already irritable myocardium.

  It can provide an option when *IV access is not readily attainable* in *urgent* situations.
- Treat any underlying cause.
- Potassium levels must be closely monitored whilst in the ED:

  ♥ ` As a general rule recheck levels every **30 minutes** for **2 hours**, then **hourly** for **4 hours**. [4]

Moderate Hyperkalemia

- This will be the same as for severe hyperkalemia, though IV calcium will generally not be needed for levels below 7.0, providing the ECG is normal.

Mild Hyperkalemia

- This is a very common presentation to the ED.

  Mild hyperkalemia cases will not need monitoring, if the initial ECG is normal.

  This can generally be treated with Resonium and correction of the underlying cause.

Special Considerations

1. Digoxin toxicity:

   - In hyperkalemia due to digoxin overdose the use of calcium is theoretically hazardous, though in practice this does not seem to be a concern.

     The treatment in this situation is **FAB fragments.**

2 Addison's disease:

- In hyperkalaemia due to Addison's disease, caution must be used when using insulin, as there is a tendency to hypoglycemia in this condition.

  The use of insulin without adequate administration of glucose may result in severe hypoglycemia.

  The mainstay of treatment in these cases is **corticosteroid**. [3]

  Specialist endocrine advice should also be sought.

Disposition

Moderate to severe hyperkalemia:

For moderate to severe cases patients must be closely monitored by ECG in the ED, until levels have reached a safe value i.e. around 6.5 mmol/L or less with stabilization of the ECG.

Patients can then be admitted for ongoing monitoring/ investigation to ward telemetry/ SSU/ HDU as appropriate.

Mild hyperkalemia:

Not all cases will require admission, however careful assessment for underlying causes must be sort and a clear disposition plan must be formulated.

In general terms:

Admission considerations in mild cases:

- If there is associated acute or acute on chronic renal failure admission is required.
- **Dialysis dependant patients should generally be admitted for their treatment.**
- **A short stay ward admission** is appropriate for uncomplicated patients, especially whilst waiting for repeat blood tests to ensure the potassium levels have has fallen to a safe level.

Discharge considerations in mild cases:

- Uncomplicated patients can be regarded as safe for discharge when the K is < **6.0 mmol/L** and the underlying cause has been corrected.
- As with all discharge considerations however these patient's social circumstances, co-morbidities, level of understanding and access to good medical care will also need to be taken into consideration.

Review arrangements:

- A review by the patient's GP should be arranged within one week, for review and repeat U&Es.

- More complex patients may require an additional early (**within 2 weeks**) hospital out-patients appointment (either Renal or General Medicine as appropriate).

- If a timely follow-up appointments cannot be arranged then an ED review is appropriate.

Medication review:

- In general if a patient develops hyperkalemia medications that cause or that will aggravate this should be **ceased** at least until the **problem has resolved** and a **medical review** has occurred.

  The medications may be re-introduced later especially if there is compelling reasons for their use, but close monitoring will be required.

Ongoing hyperkalemia treatment:

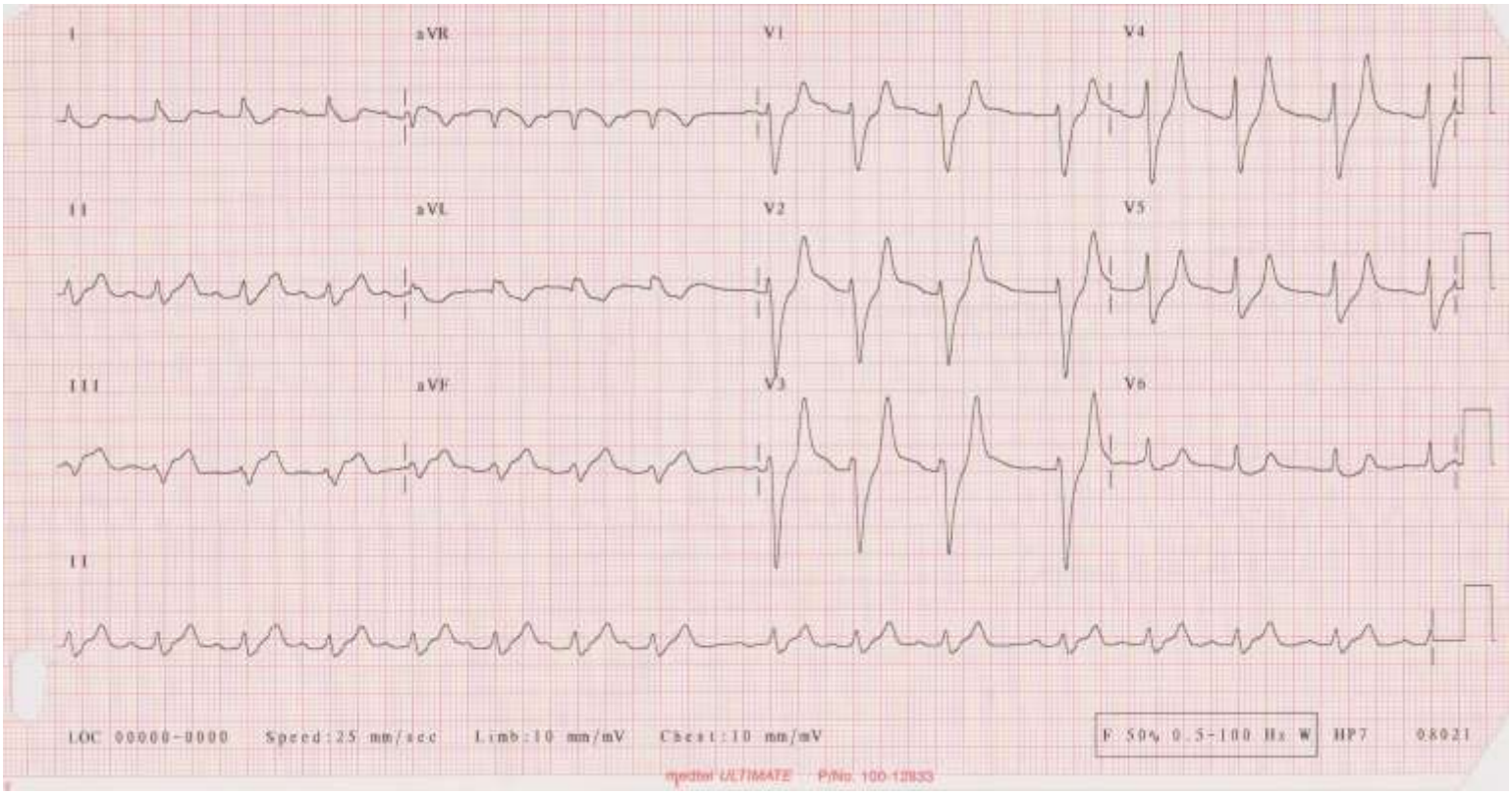
- Resonium should be continued for at least 2-3 days, or until levels have been rechecked.

Dietitian referral:

- Patients who have had an episode of recurrent or significant hyperkalemia can also be referred to the Dietitian for dietary advice.

  In general patients with hyperkalemia should avoid foods that are high in potassium such as tomatoes, bananas and any of the stone fruits.

Appendix 1



12 lead ECG of a patient with severe hyperkalemia of 8.1 mmol/L. There is peaking of the T waves and widening of the QRS complex. The P wave has not disappeared, but there is prolongation of the P-R interval, (author's ECG)

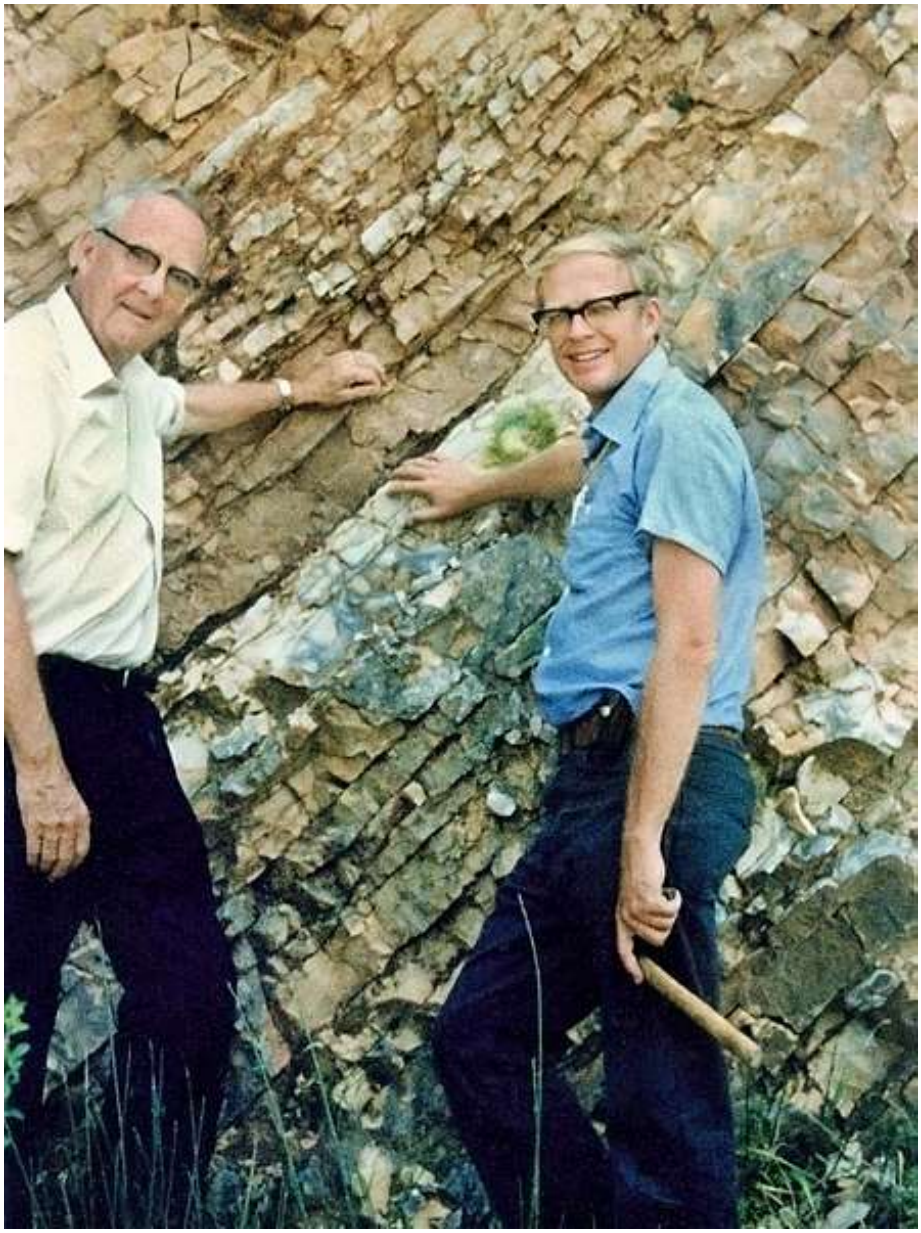
Appendix 2

Chemistry of Iridium:

Iridium, (Life Science Library, "Matter", 1963).

Iridium was named for the Greek goddess of the rainbow, Iris, on account of its colourful salts. Iridium is a rare element in the Earth's crust, however it is abundant in asteroids - a fact which led Physicist, Louis Alvarez and his geologist son, Walter to discover the cause o the extinction of the dinosaurs, 66 million years ago.

Elemental symbol:	**Ir**
Atomic number	77
Atomic weight.	192.21
Melting point	2446 ^{O}C
Boiling point	4130 ^{O}C
Classification	Metal
Physical appearance	Silvery - white.
Discovered by:	English Chemist, **Smithson Tennant** in 1803.



The brilliant father - son team of Luis and Walter Alvarez show the geological strata known as the "K-T Boundary" in Bottaccione Gorge, near Gubbio, Italy. c. 1980. This stratum is rich in the rare Earth element Iridium, normally only found in any abundance in asteroids. No dinosaur fossil has even been found in strata younger than the K-T boundary, at 65 million years old.

References:

1. Hyperkalemia: Silent and Deadly: The Lancet June 3 1989: 1240.

2. Australian Injectable Drugs Handbook 2nd ed, p. 69 & 71

3. Calcium in L Murray et al. Toxicology Handbook 3rd ed 2015.

4. eTG - March 2019

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

6. David B Mount et al. Hyperkalemia in Up to Date Website, April 2019.

Dr J.Hayes

Reviewed 23 May 2019