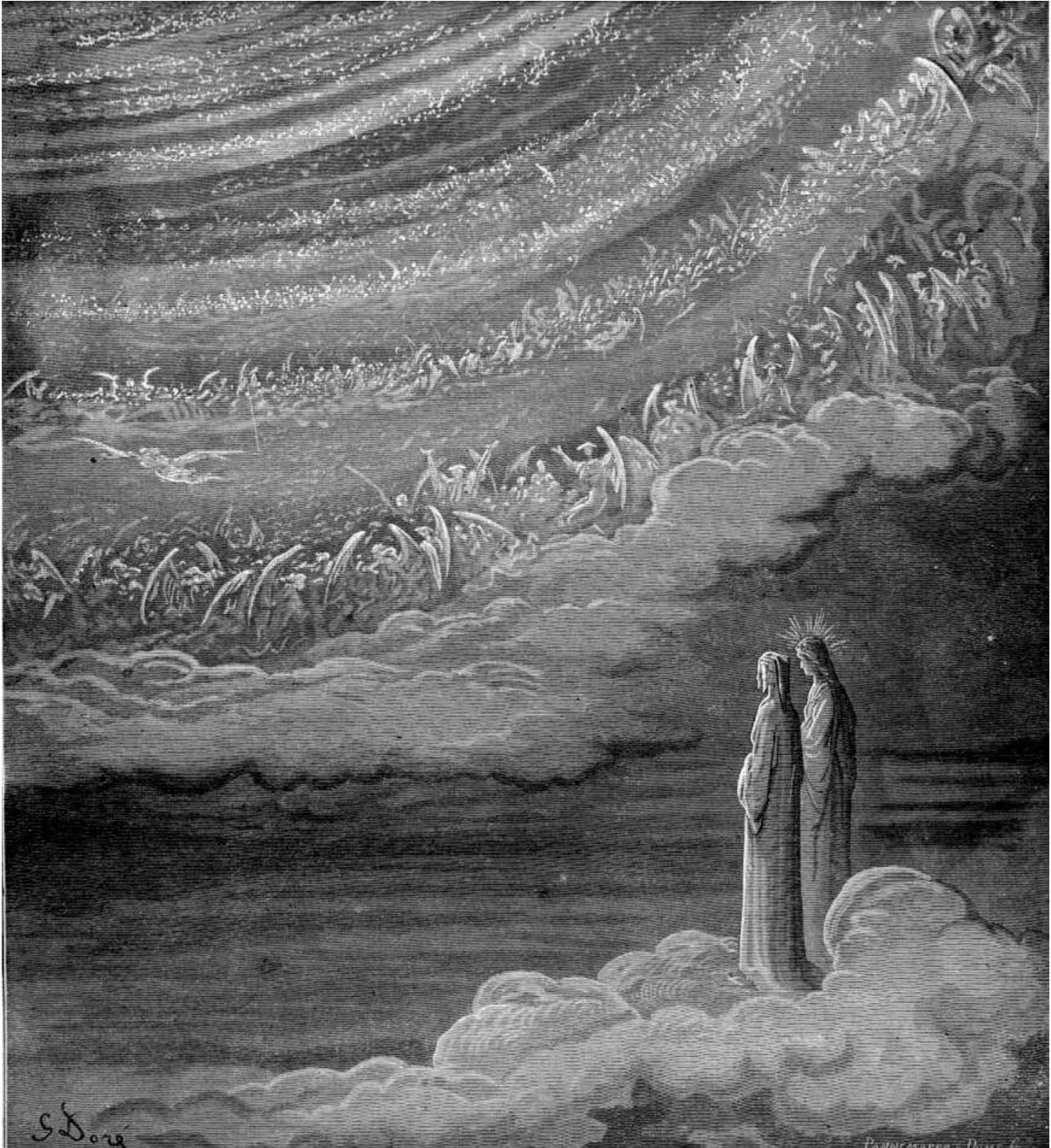


CALCIUM CHLORIDE AND GLUCONATE



*Dante and Beatrice ascending through the heavenly spheres, Woodcut Print, 1865,
Gustave Dore*

*...Beatrice was gazing upward, my gaze fixed on her,
when, perhaps as quickly as a bolt strikes,
flies, and releases from its catch,*

*suddenly I found myself there
where my eyes were drawn to an astounding sight.
And she, from whom my thoughts could not be kept
turned to me, as full of joy as she was fair,
to say "Direct your grateful mind to God,
who has conjoined us with the nearest star".*

*It seemed to me that we were in a cloud,
shining, dense, solid, and unmarred,
like a diamond struck by sunlight.*

*The eternal pearl received us in itself,
as water does a ray of light
and yet remains unsundered and serene...*

Dante Alighieri, Paradiso, II, 22-36 (1306-1317)

After his terrifying journey through Hell and Purgatory, and having been cleansed by the waters of the Lethe and the Eunoe in the Garden of Eden, Dante now sadly takes leave of Virgil, but happily can now begin his journey with his new guide, Beatrice, into the heavenly realm of Paradise. He is surprised to learn that in Paradise there are varying levels of reward, just as in Hell and Purgatory where there were varying levels of punishment and atonement. All are blessed and equal in paradise, though it seemed that some are more blessed and more equal than others! Dante Alighieri constructed the heavens in the Divine Comedy according to the prevailing scientific model of his day. This was a pre-Copernican age and Dante, a brilliant and widely educated man, used the best available knowledge of the Universe available. All luminous objects in the sky were "stars" of one sort or another. The Sun was in fact a type of star - which of course agrees perfectly well with 21st century Astronomy. But from that point on the medieval Universe was a very different place to our conception of it. All of these stars were arranged according to the ancient Ptolemaic hierarchy of ever more highly placed "crystalline spheres", each great sphere containing its own particular star or set of stars, and each rotating majestically around the Earth.

There was no concept of a heliocentric Solar System, as all the planetary "stars" circled around the Earth, and not the Sun. The Moon and the Planets were also "stars" but of special types. The Moon was very large star. It was also the closest "star" to the Earth, so at least in this sense, agreed with 21st century Astronomy. Dante finds the souls of the first celestial sphere within the sphere of the Moon, "...It seemed to me that we were in a cloud, shining, dense, solid". The Sun, for reasons unknown, was considered to lie between the planets Venus and Mars. The term planet was used, but there was no concept of a planet in the sense of the 21st century concept of another world. Instead the planets were wandering "stars" in distinction to the "fixed stars" of the eighth celestial sphere. The stars of the eighth sphere of course rotated around the night sky, but they were

*“fixed” in the sense of their positions being fixed in relation to each other, and so forming the recognizable and seemingly eternally unalterable constellations. The wandering “stars” on the other hand followed their own path along the zodiac, completely independently of the fixed stars, as they resided in their own individual different celestial spheres, separate from the spheres that carried all of the fixed stars. The order of the planets i.e. Mercury, Venus, Mars Jupiter and Saturn, was the same as modern Astronomy, as the ancients had established the **relative** distances between them, even though they had no concept at all of the actual immense distances involved, or their positions in relationship to the Earth and the Sun. Within this framework of ancient Ptolemaic Astronomy Dante weaved his vision of Paradise. According to the merit of the soul it was placed within a hierarchy of one of the celestial spheres, beginning with that of the Moon, then Mercury, Venus, the Sun, Mars, Jupiter and Saturn. The eighth sphere was that of the fixed stars - agreeing with modern Astronomy that the (true) stars were further away than the wandering stars (or planets), although just exactly how much further away no medieval mind could have possibly imagined. The ninth outermost sphere contained no planets or stars, but instead was a vast crystalline sphere known as the “primum mobile” or the “prime mover”, the “first cause” which was the engine that, by the power of God, drove the rotation of all the other spheres. Outside of the celestial spheres was the “empyrean” - a place, like the quantum world of 21st century physics, beyond the understanding of the human mind - a place that lay outside of space and of time. Other cultures at other times have had other names for this realm, Paradise, Nirvana, El Dorado, the Elysian Fields, Xanadu - in the Christian tradition, Heaven, the place of God.*

Inseparable from all this science, was astrology and religion, indeed all three were considered aspects of the same thing. Dante associated each of the heavenly spheres with classical, biblical and archaic medieval symbolism now largely incomprehensible to the modern mind. But part of his brilliance was the blending of science with faith, which presented to the medieval mind a credible, yet terrifying spectre, so credible indeed, that the political and religious authorities banned his works for the challenges they presented to their own authority. Over two centuries after Dante’s death, an obscure Polish Astronomer, by the name of Nicolas Copernicus in 1543, published an astonishing booklet, “De revolutionibus orbium coelestium” (On the Revolutions of the Celestial Spheres) that would finally shatter the ancient Ptolemaic view of the Universe. In the Seventeenth century Galileo would use the newly invented telescope to show that the planets were not stars at all, but worlds like the Earth. As Huxley would be Darwin’s ‘bulldog’, so Galileo would be bulldog for Copernicus, an heretical stance which sent him straight to the Inquisition, courtesy his hitherto great friend, Pope Urban VIII. In 1687 Isaac Newton stood on the shoulders of giants and published the Principia and nature took over the task of the “prime mover” from God. In the early 20th century Albert Einstein took us further than ever before, into a world as strange and as awe inspiring as the empyrean itself!

*In the 21st century, we have two preparations of the element calcium available for intravenous use. Each contains one gram of a salt, one chloride, one gluconate. But like the heavenly spheres of Dante not all are blessed to the same degree! The chloride preparation is closer to the “empyrean” than is the gluconate, being three times more blessed in the amount of **elemental** calcium it contains, compared to its partner.*

CALCIUM CHLORIDE AND GLUCONATE

Introduction

Calcium is an essential element for the normal physiological function of the body.

As an IV pharmacological agent, calcium is available as a:

- **Chloride**
- **Gluconate**

The calcium chloride preparation contains roughly 3 times the amount of elemental calcium compared to the gluconate preparation.

Indications for calcium therapy in the ED include:

- **Hyperkalaemia**
- Hypermagnesaemia (usually iatrogenic)
- Hypocalcaemia
- Calcium channel blocker overdose
- Hydrofluoric acid exposure, (both local and systemic).

Physiology

Calcium is an essential element for life.

It is vital for the functional integrity of the nervous, muscular (cardiac, smooth and skeletal) and skeletal systems.

It is required for the normal function of cell membranes in general.

It is an important activator in many enzymatic reactions and is essential to a number of primary physiologic processes including the transmission of nerve impulses; contraction of cardiac, smooth and skeletal muscle.

It has an important role in blood coagulation.

Calcium is an important structural element of bone and is in a constant exchange with the plasma calcium.

The normal total serum calcium concentration is **2.1-2.6 mmol/L**

Preparations

There are two principle IV preparations of calcium that are used in the ED:

- Calcium chloride:

- ♥ 10 % in 10 ml ampoule

This is equal to **1 gram** of calcium gluconate in each 10 ml ampoule. The actual amount of **elemental** calcium is **6.8 mmols** per 10 ml ampoule.

- Calcium gluconate:

- ♥ 10 % in 10 ml ampoule

This is equal to **0.935 gm** of calcium gluconate in each 10 ml ampoule. The actual amount of **elemental** calcium is **2.2 mmols** per 10 ml ampoule.

Note therefore that the calcium chloride preparation contains roughly 3 times as much elemental calcium as does the calcium gluconate preparation.

- Calcium gluconate **gel, 2.5 %** for topical administration (for HFl burns).

Mechanism of Action

Calcium acts as a physiological antagonist to cardiac and skeletal muscle effects of:

- Hyperkalaemia
- Hypermagnesaemia

In hydrofluoric acid poisoning calcium binds to fluoride ions to prevent further tissue penetration and injury.

Pharmacokinetics

Absorption:

- Therapeutic calcium is given intravenously.
- Nebulized calcium can also be given in cases of HFl inhalational injury.
- Topical calcium can be given for HFl skin burns.

Distribution:

- 99 % of the calcium in the body is contained within bone.

- Of the calcium that is in plasma, half of this is ionized and physiologically active.
- About half of the calcium in plasma is bound to albumin.

Metabolism and excretion:

- Calcium metabolism is very closely regulated by the body principally via parathyroid hormone, calcitonin and vitamin D.

Calcium is excreted mainly in the faeces and consists of unabsorbed calcium and that which is secreted via bile and pancreatic juice into the lumen of the GI tract. Most of the calcium filtered by renal glomeruli is reabsorbed in the ascending limb of the loop of Henle and proximal and distal convoluted tubules. Only small amounts of the cation are excreted in urine.

Indications

Indications for calcium therapy include:

- **Hyperkalaemia**
- Hypocalcaemia
- Hypermagnesaemia (usually iatrogenic)
- Calcium channel blocker overdose
- Hydrofluoric acid exposure, (both local and systemic).

Both the chloride and gluconate preparations are used for IV administration.

The gluconate preparation can be used subcutaneously or via nebulized inhalation in cases of HFI exposure.

Contra-indications/precautions

These include:

- Hypercalcaemia
- Digoxin toxicity:

This is a controversial issue and is probably now more regarded as a theoretical contraindication, though in practice it seems safe to give in this setting with caution.

Pregnancy:

Calcium is safe to give in pregnancy.

Breast feeding:

Calcium is safe in breast feeding.

Adverse Effects

Adverse effects include:

1. Transient hypercalcaemia:
 - Tetany / seizures may occur.
Cease administration and check calcium levels.
2. CVS:
Excessively rapid and/or excessive dosing may lead to:
 - Hypotension
 - Arrhythmias (including cardiac arrest)
3. Calcium **chloride** can cause tissue necrosis if extravasated.

Dosing

Patients who are receiving IV calcium should be on continuous ECG monitoring.

For hyperkalaemia or hypermagnesaemia or severe/ symptomatic hypocalcaemia: ¹

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)

The effect is relatively short-lived and the dose may need to be repeated in 10-15 minutes as required.

See also separate documents on Hyperkalaemia, Hypermagnesaemia, and Hypocalcaemia (in Renal and Electrolytes folder).

For calcium channel blocker overdose

Note that for significant calcium channel blocker overdose the principal treatment will be **Insulin-Dextrose euglycaemia therapy.**

Calcium therapy will only be adjunctive therapy.

The administration of calcium to increase extracellular calcium appears to at least partially reverse the heart block and arrhythmias induced by calcium channel blocker overdose usually found with verapamil or diltiazem.

In patients with heart block or cardiac dysrhythmias, use: ¹

- **Calcium chloride: 2 grams (20 mls) IV over 5-10 minutes.**

Or

- **Calcium gluconate: 6 grams (60mls) IV over 5-10 minutes.**

This dose may be repeated every 20 minutes for up to 3 doses.

If there is a response to calcium then an infusion may also be considered: ³

- **Calcium gluconate 10% 3 to 30 mL/hour (child: 0.06 to 0.6 mL/kg/hour) IV peripheral infusion**

Or

- **Calcium chloride 10% 1 to 10 mL/hour (child: 0.02 to 0.2 mL/kg/hour) IV infusion by a central line.**

Serum calcium levels should be monitored. A calcium concentration of 2 mmol/L has been suggested as optimal.

See also separate document on Calcium Channel Blocker Overdose (in Toxicology folder).

For HFL acid exposure:

Topical 2.5 % gel can be given as immediate first aid.

Calcium gluconate (but **not** the chloride preparation) can be infiltrated in the subcutaneous tissues.

Calcium **gluconate** can be used for Biers Block or intra-arterial infusions.

Large doses of calcium **chloride** may be required to maintain calcium levels in cases of severe HFL systemic poisoning.

See also separate document on HFL exposure (in Toxicology folder).

*Dante based his Universe on the pre-Copernican, Ptolemaic construction of the heavenly
“crystalline spheres” (From “Reading Dante”, Prue Shaw).*

References

1. Calcium in L Murray et al. Toxicology Handbook 3rd ed 2015.
2. Australian Medicines Handbook, Website Accessed April 2015.
3. eTG - March 2015
4. Calcium Chloride Injection in MIMs 1 March 2014.

Dr J. Hayes
May 2015.