The knowledge and practice of emergency department doctors in the management of calcium channel blocker overdose in South Africa

BY

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Contents

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12 July 2023

I would like to dedicate this to my loving soon to be husband, Marcio Caldeira. Thank you for being my rock and for always encouraging me to be the best. You are my person, I love you
- *Brunfelsia pauciflora*

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Abstract

Background

Calcium channel blocker (CCB) overdose (OD) has the highest mortality rate in comparison to other cardiovascular agents. The treatment of a severe CCB OD is challenging for emergency doctors with limited literature even in developed countries. It is important that in the South African (SA) setting that good knowledge and awareness of emergency doctors on CCB OD's and their clinical presentations, would produce fewer patient mortalities.

Objectives

To explore the knowledge and practice of SA emergency department (ED) doctors, in both public and private sectors, in the management of CCB OD as well as barriers and facilitating factors they encounter when managing such patients.

Methods

A cross-sectional study was conducted among South African emergency medicine doctors using a self-administered electronic survey. The survey contained 39 questions including demographics and a combination of open, closed, case-based and Likert-scale based multiple-choice questions as adapted from *Brassard et al.*

Results

A total of 119 doctors participated in the survey, 59 were state medical officers (MO), 30 were registrars and 30 worked in private EDs. The mean (SD) age of participants was 32.9 years (6.4). The mean knowledge (SD) score of all participants was 54% (13.3), which was the lowest for public MOs (48%) and significantly higher for private MOs (58.4%) and registrars (60.1%). Forty eight percent of participants didn't know of any guidelines to treat a CCB OD. Current practice of EM doctors showed that fifty-five percent of the group would initiate HIET along with a vasopressor for CCB induced shock. Barriers to managing a CCB OD were highlighted with unavailability of infusion pumps, understaffing in the unit, and a full resuscitation unit being the most common with no significant differences between the subgroups. Thirty seven percent of participants agreed that the most popular facilitating factor was having past experience when managing a CCB OD.

Conclusion

This study has highlighted the need to address ED doctor knowledge gaps on CCB OD management, further emphasising the importance of clinical toxicology education in South Africa. Guidelines are needed to improve EM doctor practices to ameliorate patient outcomes.

Introduction

Calcium channel blocker (CCB) overdoses are responsible for more fatalities than any other cardiovascular agent in the USA, with an estimated 42% mortality rate in one report.[1] Hypertension has a prevalence rate of 30.4% in South African (SA) adults and CCBs are one of the recommended first-line therapeutic agents.[2] CCBs are, therefore, found in many SA households and could lead to overdose (OD).[3,4] Deliberate self-poisoning is a significant public health issue in developing countries[3] and more studies need to be undertaken in SA to improve patient care and outcomes.
The treatment of a severe CCB OD can be challenging for emergency doctors as often a multimodal therapeutic approach is needed. [5] Such an approach can be divided into supportive treatments; which include airway, breathing and circulation management; and specific treatments, such as intravenous calcium, vasopressors, and high insulin euglycaemic therapy (HIET). International and SA guidelines have encouraged the use of HIET in severe CCB OD's. An international expert consensus guideline was published to assist in the treatment of CCB OD's thereby reducing discrepancies in physician practice. Following such a guideline has also shown improvements in cardiac output, blood pressure and possibly increases in survival. [6]

International literature on the physician management of CCB poisoning is limited to developed countries. In Canada, only 42% of CCB poisonings are managed according to the poison control advice due to a lack of physician training in managing overdoses as well as limited resources, which ultimately impacts patient care.[7] An SA study done on deliberate self-poisoning cases concluded that good knowledge and awareness of emergency department health professionals on common poisonings would produce fewer patient morbidities and mortalities.[3] A knowledge and practice survey can be used to assess whether doctors working in Emergency departments know of and adhere to guidelines in the management of CCB poisoning.[11]

A knowledge and practice study was therefore performed to understand the current knowledge and practice of emergency department (ED) doctors in the management of CCB OD as well as the specific use of HIET. Differences in knowledge and practices between doctors working in private and state departments were sought as well as between doctors of varying experience. Barriers and facilitating factors to the management of CCB OD were also studied with the aim to identify specific factors which were either lacking, needed improvements or to guide the future implementation of protocols. [11]

Methods

Study Design
This was a prospective observational cross-sectional study.

Participants and setting
The study population was a convenience sample in South Africa, consisting of three groups: emergency medicine registrars, emergency medicine doctors working in private emergency departments and medical officers (MOs) working in Emergency Departments (ED) in state hospitals in Gauteng. All ED doctors willing to participate in the study were included and doctors working in other departments and incomplete surveys were excluded. Sample size calculation was based on the 5% significance level, 80% power and medium effect sizes (Cohen's d=0.4), for three subgroups, using paired statistical tests. This resulted in a sample size estimation of 90 participants, 30 in each subgroup. Sample size calculations were carried out in G* Power.

Data Collection

An electronic survey using SurveyMonkey®, was distributed via email and social media advertising (Supplementary appendix A). In-person visits to both state and private emergency departments were also done to invite interested medical officers and registrars to complete the survey by sending them a survey link. The survey was self-administered.

Once the survey was completed, the participants were invited to watch an online Continuous Professional Development (CPD) accredited webinar on the management of CCB OD at their discretion. This would help bridge the gap in the doctor's knowledge in management of CCB OD's after taking the survey. The anonymity of the survey remained as this occurred after the survey was taken and we had no access to who watched the webinar.

Informed consent was assumed by participants if they completed the online survey. The survey contained 39 questions with a combination of open, closed, case-based and Likert-scale based multiple-choice questions as adapted from *Brassard et al.*, (Supplementary appendix B).

Data analysis

The data was exported onto a spreadsheet (Microsoft Excel, Microsoft Office 365, Microsoft Corporation). SPSS® Statistics version 27 was used to analyse the data. Descriptive statistics for parametric variables of the sample population was used. For some parametric data, a Chi-squared test of independence was performed, using a contingency table, to assess whether two variables were independent or associated with each other. Closed-ended questions for knowledge were scored according to a memo (Supplementary appendix C). The total score was analysed by comparing the percentages scored of the three sample groups, using means. A one-way ANOVA was then used to demonstrate differences between the mean score of the groups. A Levene's test was done with a p value of 0.035, thus the Dunnett T3 post-hoc/multiple comparison test was used. The Kruskal Walis test was used for unpaired non-parametric data. The open-ended questions were scored according to a memo, or they were analysed qualitatively by finding and describing common trends among the responses. This data was tabulated, and frequencies and column percentages were used. Significance testing was set at the 95% confidence level with a p-value < 0.05 indicating statistical significance.

Ethical considerations

The study was approved by the Witwatersrand University Human Research Ethics Committee (ref.no. M201053). Anonymity of the participants was maintained throughout the study process and data was only accessible to the researchers.

Results

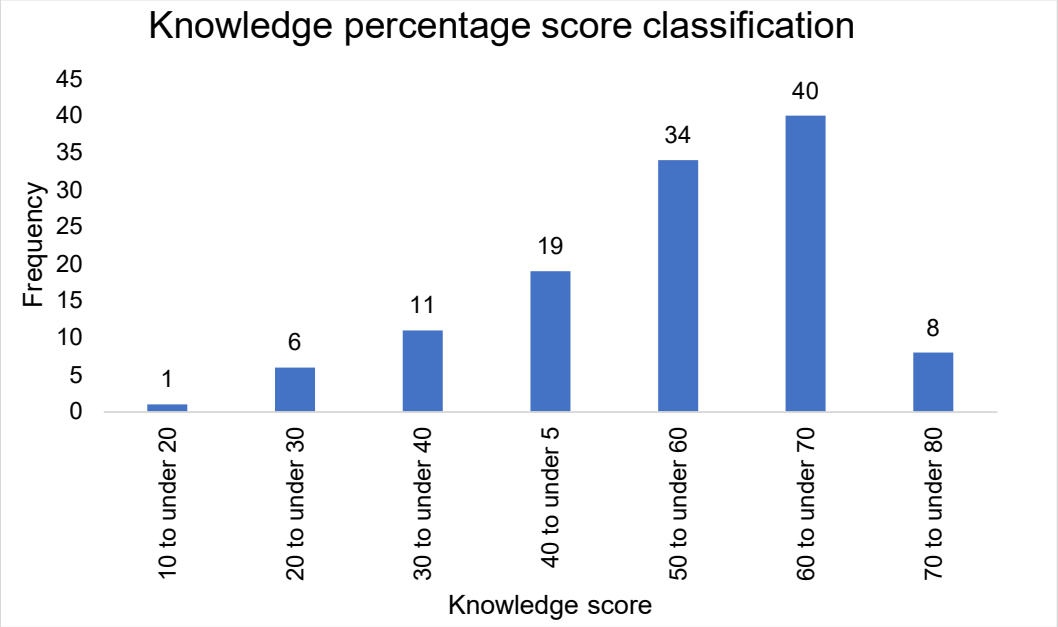
Demographics

A total of 119 doctors participated in the survey, of whom 59 were state MOs, 30 were registrars and 30 were doctors working in private EDs. The mean (SD) age of participants was 32.9 years (6.4), and the average years of experience was 4.7 years (3.7). Over the past year, 42% of the sample population had not treated a CCB OD; 22.7% had only treated one and 35.3% had treated two or more. Of note, 60% of doctors working in the private sector had not treated a single CCB OD while the 56.7% of the registrar group had managed 2 or more CCB ODs within the past year, $p=0.003$. Forty-five percent of the group had used HIET in CCB OD management before, with more registrars than public MOs and private MOs having experience with HIET: 83.3% versus 32.2% and 33.3% respectively, $p < 0.001$.

Knowledge

The mean knowledge score of all participants was 54% (13.3) with 33.6% of the overall group scoring between 60 to 70 percent. See figure 1. The mean knowledge score was the lowest for public MOs (48%) and significantly higher for private MOs (58.4%) and registrars (60.1%). There was a significant statistical difference in mean scores between registrar subgroup versus the public MOs; as well as private MOs versus the public MOs, $p < 0.001$ and $p=0.002$. There was no statistical significance between knowledge score and different years of experience ($p=0.066$).

Figure 1. Distribution of knowledge scores for the group overall



When asked which guidelines they use to treat a CCB OD, 48% of the group didn't know of any guidelines. Of those participants who did utilise guidelines, the most commonly used were either international guidelines, the EM guidance app or a combination of resources, see table 1 below. Most of the registrars (96.7%) responded that they learnt about HIET while working in the ED rather than from journal articles, textbooks, or medical school. See table 2.

Table 1. Guidelines used to treat a CCB OD

Total (n=119)		**Private (n=30)**	**Public (n=59)**	**Registrars (n=30)**
Unsure/I don't know	48.7%	46.7%	54.2%	40%
Afritox	0.8%	3.3%	0%	0%
International guidelines	10.1%	13.3%	5.1%	16.7%
EM guidance	7.6%	13.3%	8.5%	0%
Hospital/ED guidelines	3.4%	3.3%	5.1%	0%
Life in the fast lane	4.2%	3.3%	5.1%	3.3%
NDoH guidelines	1.7%	3.3%	1.7%	0%

SAMJ article, Stephen et al.	5%	3.3%	3.4%	10%
Other	5.9%	3.3%	10.2%	0%
More than 1 source	8.4%	3.3%	3.4%	23.3%
None	4.2%	3.3%	3.4%	6.7%

Table 2. Where did ED doctors first learn about HIET

Total (n=119)		**Private (n=30)**	**Public (n=59)**	**Registrars (n=30)**
Working in ED	68.9%	56.7%	61%	96.7%
Journal article	5%	13.3%	3.4%	0%
Colleagues	4.2%	10%	3.4%	0%
Medical school	2.5%	0%	5.1%	0%
Textbook	2.5%	0%	5.1%	0%
I haven't heard about it before now	12.6%	6.7%	22%	0%
Other	3.4%	10%	0%	3.3%

Practices

When asked about their current practice in managing CCB OD, 29.4% of the group as a whole would start a vasopressor as the sole form of cardiovascular support. Of the subgroups, only 3.3% of registrars would initiate this therapy alone while 33.9% of public MOs and 46.7% of private MOs would initiate a vasopressor as monotherapy, $p < 0.001$. (In Pearson chi square test resulted in 60% of cells having an expected count less than 5 therefore interpret p-value with caution) Fifty-five percent of the group would initiate HIET along with a vasopressor for CCB induced shock, with more registrars (93.3%) choosing this practice compared to public MOs (44.1%) and private MOs (40%). Starting HIET as monotherapy for CCB induced shock was selected by just 5.9% of the group as a whole.

When questioned regarding their choice of vasopressor/inotrope, 97.5% of ED doctors chose adrenaline. Dopamine (0.8%) and noradrenaline (1.7%) were less preferred by the group. When asked about whether they seek advice on the management of CCB ODs, 63.9% of participants stated they would consult an EM physician for advice in comparison to just 11.8% who would rather consult a poison centre, and 9.2% who would ask a more senior doctor on the floor, $p = 0.03$.

Barriers and facilitating factors

The barriers and facilitating factors to managing CCB ODs and initiating HIET are described in table 3. The most common barrier was the unavailability of infusion pumps (60.5%) followed by understaffing in the unit (42.9%), the resuscitation area being full (32.8%) the lack of an available consultant (26.9%) and the ED being busy (24.4%). There were no significant differences between the subgroups. General facilitating factors included not receiving criticism from colleagues when using HIET and past experience with CCB OD's.

Table 3. Barriers and facilitators to initiating HIET in a CCB OD

Factors	Total (n=119)	Private (n=30)	Public (n=59)	Registrars (n=30)	p value
General Barriers					
Unavailable Consultant	26.9%	30%	32.2%	13.3%	0.150
Lack of ICU beds	9.4%	33.3%	32.2%	20%	0.422
Unable to call poison centre	5.9%	6.7%	8.5%	0%	0.269
CVP confidence	11.8%	13.3%	13.6%	0%	0.605
Busy ED	24.4%	30%	23.7%	20%	0.657
Full Resuscitation beds	32.8%	30%	32.2%	36.7%	0.852
Unavailability of infusion pumps	60.5%	53.3%	59.3%	70%	0.404
Understaffing in the unit	42.9%	43.3%	37.3%	53.3%	0.351
General Facilitators					
Lack of criticism from colleagues when using HIET	13.5%	3.4%	3.4%	6.7%	< 0.001
Past experience with CCB OD affect decision to initiate HIET	37.8%	46.7%	20%	66.7%	< 0.001

Participants who had used HIET before were asked to describe barriers that hindered ease of use of HIET in their setting as well as any facilitating factors, see table 4. Availability of resources, concerns about complications arising from HIET, staff reluctance and lack of familiarity with HIET were the most common barriers for the group overall. Availability of resources was described as a barrier less often for Private MOs (20%) versus public MOs (47.5%) and Registrars (50%). A common facilitating factor for those in the private sector, who had used HIET before, was a previous experience of using HIET without complications. (40%). The lack of criticism (13.5%) from colleagues when using HIET was seen as a facilitating factor too.

Table 4. Barriers and facilitators for those who have used HIET before in a CCB OD

Barriers	Totals (n=53)	Private (n= 10)	Public (n= 19)	Registrars (n= 24)
Availability of resources: a) IV lines b) HC/ICU beds c) Infusion pumps d) Staffing e) Difficulty with calculation of doses and infusion rates	43.5% a) 5.7% b) 3.8% c) 9.4% d) 13.2% e) 11.3%	20% a) 0% b) 0% c) 0% d) 10% e) 10%	47.5% a) 15.8% b) 5.3% c) 15.8% d) 5.3% e) 5.3%	50% a) 0% b) 4.2% c) 8.3% d) 20.8% e) 16.7%
Staff reluctance	32.1%	20%	26.3%	40.7%

HIET unfamiliarity	24.5%	10%	15.8%	37.5%
Frequent monitoring	18.9%	0%	21.1%	25%
Initiating HIET late	1.9%	0%	0%	4.2%
Complications of HIET a) Hypoglycaemia b) Fluid overload c) Hypokalaemia	37.4% a) 17% b) 11% c) 9.4%	10% a) 10% b) 0% c) 0%	36.9% a) 21.1% b) 10.5% c) 5.3%	50.1% a) 16.7% b) 16.7% c) 16.7%
Takes time to initiate	3.8%	10%	0%	4.2%
Facilitators				
None: No problems	17%	40%	15.8%	8.3%

Discussion

This is the first formal assessment of ED doctors on their knowledge and practices in managing a CCB OD in SA, and to our knowledge the only study reported from Africa. There are a few major findings, some which are consistent with studies from developed countries and some which are unique to our SA setting.

The mean knowledge score was 54% which is slightly higher than an international study done by Monteith *et al*, with participants scoring 45.2%.[9] Monteith *et al* also showed that EM trainees, our registrar equivalent, scored significantly better with 82.3% in comparison to CMOs (chief medical officers) with 65.4%.[9] This comparison between the different sectors was also seen in our study and shows a lack of knowledge as well as difficulty in knowledge application especially in the public setting. Marks *et al* highlighted that high mortality rates in acute poisonings is due to numerous factors, one being poor medical care, including the lack of toxicological expertise among health care providers.[10] Maude St-Onge emphasised that in managing unstable poisoned patients, doctors often report cognitive overload, and that better knowledge of cardiovascular drug toxicity would improve patient outcomes.[11] In our study there were practicing specialised EPs (emergency physicians) in both private and public ED's, and we postulated that the public MO's had less academic exposure. In comparison, registrars train in emergency medicine for four years full time in an HPCSA-approved training post in academic institutions where the academic and clinical aspects of emergency patient care are emphasised and thus the registrars were expected to score above average on the knowledge component of the survey.[12]

However, Bush *et al* highlighted that even Emergency Medicine residents were less confident being tested on and in managing CCB toxicities.[13] A large proportion of our participants had not treated a CCB OD, even more so those doctors working in the private sector. Van Hoving *et al* showed that cardiovascular medicine was the second highest toxin ingestion with 12.8% of patients presenting to a SA public ED. [14] It is possible that private patients present with different parasuicide ingestions compared to what is seen in state hospitals however, no data is available, and more research is needed in the private health sector.

According to *Maude-St Onge et al*, there is an absence of formally recognised guidelines in the management of CCB poisoning internationally [6], this was also translated in our study with 48.7% of the group not knowing about any guidelines. Clinical toxicology forms part of EM and new diagnostic and treatment methods are constantly being developed and updated.[15] The need for standardised and updated guidelines was highlighted by Chiew *et al*; that clinicians treating poisoned patients need an up-to-date accessible resource to aid their management decisions using evidence-based medicine.[16]

The importance of guidelines in our SA setting is that this resource can be used by non-expert clinicians such as junior doctors or those based rurally in to provide best medical

therapy to poisoned patients.[16] One of the platforms available to overcome this challenge are mobile medical applications. A South African study done by Kabanda et al, found that 87% of EM doctors used medical applications installed on their mobile devices to access instant clinical guidelines.[17] Afritox® is a software system to help SA doctors to diagnose and treat poisonings however, it was used by only 0.8% of the group. This could be due to Afritox® Online requiring a personal annual subscription or that Afritox® Offline requires a working computer, which is not always available in the state sector and an annual subscription for private hospitals is required.[18]

The current literature for the management of CCB toxicity is limited with low to very low quality of evidence available.[11] An expert consensus in 2016 summarised first line therapies for CCB poisoning which included calcium administration, the use of adrenaline or noradrenaline and HIET.[6] A low percentage of our participants would start both inotropic support and HIET as well as refer to the ICU, which shows that the majority are not aware that HIET should be initiated early. This was also shown in Brassard *et* al's study where HIET therapy had the lowest adherence rate and that 38.9% of clinicians would rather use vasopressors than early HIET initiation.[19] It is important to note that 83.3% of registrars were more comfortable in starting HIET early when compared to public MO's (32.2%) and private MO's (33.3%). This could be due to their academic teaching, rotations through ICU's or possibly more experience (56.7%) of having managed more than two CCB ODs over the past year. The selection of vasopressors used in a CCB overdose should be guided by the type of shock [11] thus both noradrenaline and adrenaline are recommended. Most of the group opted to use adrenaline, which is readily available in all SA ED's as it is freely available. For the small percentage of the group who opted for noradrenaline, it was either private or registrars as it is not widely available in the public sector.

Most participants would call an EP for advice on managing a CCB OD, which according to Monteith *et al* 70.4% of consultant EM physicians were confident in managing these patients.[9] A very low percentage of ED doctors would consult a poison control centre (PCC) when having to manage a CCB OD. According to the WHO, PCCs are a scarce resource in most African countries with only 17.2% of African countries having a PCC.[10] SA only has three Poisons Information Centres in the public sector, two of which are situated in the Western Cape.[20] Such resources are underutilised in SA and would assist with best practices in managing acute poisoning and help in data collection for toxicovigilance and surveillance.[20]

In our study we identified a myriad of barriers. ED's worldwide are notorious high-stress environments due to large patient volumes, limited resources and overcrowding.[21] Infusion pumps were the resource reported as most frequently lacking; which according to Balaeni et al only 53.9% of African clinicians always had access to syringe pumps in comparison to 100% of high income countries.[22] For participants who had used HIET before, availability of resources was found to be better in the private sector than in the public sector. This is evidenced by SA having an unequal two-tiered health system; with a very well-resourced private sector servicing 16% of our country's population and a poorly resourced public sector who serves 84% of the population.[23,24] Moreover, the Human Science Research Council (HSRC) disclosed an additional inequality with 59% of medical doctors working in the private sector and only 41% working in public.[23] It can be postulated that departments in the private sector function similarly to developed countries and public with that of a developing county. In a comparative Canadian study, 28% of participants stated they had experienced general resource limitations when initiating HIET.[19] Understaffing in South Africa is common, and the healthcare profession has learnt to adapt to such circumstances. However, it is sometimes impossible without adequate staff to give the best patient care. HIET is very labour intensive and without adequate staff or resources, it is impossible to implement safely. Furthermore, it is difficult to implement without the cooperation of colleagues who may be sceptical of the treatment. Statistics from the Organisation for Economic Co-

operation and Development (OECD) show that SA healthcare is severely under-resourced with 0.79 doctors per 1000 inhabitants in comparison to the world average of 3.37 in 2019.[25] Even in comparison to low-income countries, SA ranks only slightly above them.[26] South African government has now added specialist medical posts, including EM specialists to the critical skills list in August 2022 to avert this growing medical staff shortage.[27]

Overcrowding in EDs is a worldwide public health issue, which has many confounding factors as causes; one being an increase in toxicology-related ED visits which are resource-intensive and have longer lengths of ED visits or hospital admissions.[28] Furthermore, resuscitation efforts are delayed with overcrowding as staff are overburdened with patients leading to poorer clinical outcomes and increased patient mortality.[29] Van Hoving *et al'*s study on self-poisoning in the ED of Khayelitsha Hospital showed an OD with amlodipine stayed the longest, 1350 minutes, in their resuscitation unit.[14] Consequently, policy makers and health officials need to grasp the importance of the burden of toxicology in clinical medicine in order to implement clinical toxicology courses which can be available for health care workers; maintain and establish effective PCC's as well as to employ clinical toxicologists to assist with policies to manage poisoned patients to improve public health.[30] In order to further reduce self-harm incidence, the WHO recommends strategies for recognition and management of mental health disorders as well as primary prevention, including psychological and social support in communities.[31] Facilitating factors in initiating HIET in our study was that participants did not receive criticism from colleagues when using HIET and past experience with CCB OD's; which is comparative to Canadian literature which showed 17% and 39% respectively.[19]

Limitations

This survey data collection was started at the beginning of the COVID-19 third wave in SA and could have been a confounding factor as a tremendous amount of pressure was placed on all emergency departments resulting in a low response rate to the survey. This added to the non-respondent bias, with either participants not initiating the survey from the email sent or many incomplete entries of the survey. Data for surveys requiring prompting was not collected which could attribute to response bias. Furthermore, the covid-19 pandemic changed the pathology of patients presenting to the ED, which may explain why doctors in the study had seen fewer CCB ODs during the previous year.

Conclusion

Multiple barriers to managing patients with CCB OD in the ED were found which included limited resources, overcrowding and understaffing. This emphasised the importance of clinical toxicology in South Africa; and the need for EM toxicology education, effective PCC's, future recommendations for the training of clinical toxicologists, as well as mental health care to improve public health. This study has highlighted the need to address knowledge gaps on CCB OD management, especially by EM doctors working in the public sector. Meanwhile, guidelines on how to treat such patients need to be accessible and up to date to improve EM doctor practices to ameliorate patient outcomes.

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Appendix A

Social media Advert

Appendix B

Self-Administered Questionnaire

Demographics

1. **Do you work as an Emergency Department (ED) doctor?**
   - Yes: carry on with rest of survey
   - No: please stop survey

2. **What is your age? (years)**

   Insert number

3. **Which ED do you work in?**
   - Public
   - Private

4. **Are you a:**

- Community service officer
- Medical officer
- Registrar
- Other: please specify……

5. **How many years have you worked in an Emergency department?**

   Insert number

Knowledge

6. **Which of the following signs are common in a patient with toxic calcium Channel Blocker overdose? Tick all that apply**

- ☐ Hypertension
- ☐ Hyperglycaemia
- ☐ Hypotension
- ☐ Miosis
- ☐ Hyperthermia
- ☐ Depressed level of consciousness
- ☐ Hyponatraemia
- ☐ Other: please state
- ☐ I don't know

7. **What is the minimum toxic dose of Amlodipine in a 70 kg adult?**

- 20 mg
- 0,1 mg/kg
- 10 mg
- 5 mg
- I don't know

The following questions (Q8-11) relate to the following scenario:

8. **A 20-year-old female presents to the ED 12 hours after ingesting 60 tablets that were prescribed for her grandmother's hypertension. The patient's vitals are BP= 85/40 mm Hg, HR= 45 BPM, SPO2= 85% on Room Air and a GCS of 13/15.**

Which initial general measures would you start on this patient? Tick 2:

- ☐ Give activated charcoal
- ☐ Reliable intravenous access
- ☐ Gastric lavage
- ☐ Oxygenation using a non-rebreather mask
- ☐ Start an N-acetylcysteine infusion
- ☐ Cardiology consult
- ☐ I don't know

9. **After acquiring further history from the patient's escort, they show you 2 empty 10mg Amlodipine boxes. The patient repeat vitals are: BP= 84/42 mm Hg,**

HR=38 BPM, SPO2= 88% on a non-rebreather mask and her GCS has dropped to 7/15. An arterial blood gas was done and shows the following results: pH: 7.12, PaCO2: 58mmHg, PaO2: 43mmHg, Na: 140 mmol/l, K: 4.2 mmol/l, Cl: 101 mmol/l, Ca: 0.89 mmol/l, glucose: 16 mmol/l, lactate: 5.2 mmol/l, BE: -12 mmol/l, Bicarb: 8 mmol/l. What specific therapies would you now use to treat this patient? Tick all that apply:

- ☐ 2L IV fluid bolus
- ☐ Calcium replacement
- ☐ 20ml/Kg IV fluid bolus
- ☐ Sodium replacement
- ☐ Atropine boluses: up to 3 boluses in total
- ☐ Amiodarone infusion
- ☐ Adrenaline boluses: up to 4 boluses in total
- ☐ Inotropic infusion
- ☐ Intubation
- ☐ High dose insulin euglycaemic therapy (HIET)
- ☐ Glucagon boluses and infusion
- ☐ I don't know

10. The patient is now intubated and was started on an adrenaline infusion (0.5 µg/kg/hr) and HIET (1 IU/kg/hour). The nursing sister is concerned as patient's vitals are: BP=88/53 mmHg, HR=48 BPM, SPO2= 94% on FiO2 of 60% and HGT is 12mmol/l. Which of the following is most likely to improve the patient's clinical condition?

- o Increase FiO2 on the ventilator
- o Replace the patient's glucose
- o Increase the HIET to 5IU/Kg/hour and monitor blood pressure changes
- o Give 60mg of Lasix IV stat
- o Consider haemodialysis for the patient
- o I don't know

11. The patient remains hypotensive despite the adrenaline infusion and HIET, which is currently running at 10 IU/kg/hr. What other therapies could you consider administering to this patient? Tick all that apply:

- ☐ Phosphodiesterase inhibitors
- ☐ Amiodarone loading dose then infusion
- ☐ Intralipid infusion
- ☐ Cardiac pacing
- ☐ Atropine infusion
- ☐ Extracorporeal membrane oxygenation: ECMO
- ☐ Albumin haemodialysis
- ☐ I don't know
- ☐ Other: please state

12. Does glucagon play a role in treating calcium channel blocker overdose?

- o There is no role
- o There is a role, but shouldn't be first choice

- There is a role as it improves mean arterial pressure
- I don't know

13. What is the maximum recommended amount of intravenous fluid that should be given to a patient with symptomatic calcium channel blocker overdose?

- 10 ml/kg
- 20 ml/kg
- 30 ml/kg
- 40 ml/kg
- 50 ml/kg
- 60 ml/kg
- I don't know

14. What guidelines have been published to assist emergency doctors with managing a patient with a CCB overdose?

15. Explain what you understand by the term high dose insulin euglycaemic therapy (HIET) in the management of calcium channel blocker overdose?

16. Where did you first learn about HIET?

- Medical school
- Working in the Emergency Department
- Colleagues
- Social media
- Textbook
- Journal article
- I have never heard about it before now
- Other: please state

17. A 32-year-old male patient presents to your ED 8 hours post ingestion of an unknown amount of Amlodipine. His vitals are: BP= 80/58mm Hg, HR= 40 BPM, SPO2= 94% on Room Air and a GCS of 15/15. A CVP line has been inserted and adrenaline infusion started at 0.1 µg/kg/hr. The patient has already received a 20 ml/kg fluid bolus and 30 ml of calcium gluconate. When would you consider starting HIET on this patient? Select one?

- I would not start HIET on this patient
- Simultaneously with the adrenaline infusion
- Only after patient is accepted to ICU: 24 hours post ingestion of Amlodipine
- Once the patient has reached the maximum dose of the adrenaline infusion and remains haemodynamically unstable
- Only if patient requires intubation

- Once the patient has required adrenaline 0.5 ug/kg/min and remains haemodynamically unstable
- I don't know

18. Do you think there is strong evidence for the use of HIET as an effective clinical treatment?

- Yes
- No
- I'm not sure

19. What are commonly reported side effects of HIET? Tick all that apply:

- Hypoglycaemia
- Hypocalcaemia
- Hypomagnesaemia
- Hypotension
- Lactic acidosis
- Hypernatraemia
- Hypokalaemia
- Hyponatraemia
- Pulmonary oedema
- Other: please state
- I don't know

20. What is the starting dose of insulin used in HIET?

- 0.1 IU/kg/hr
- 0.05 IU/kg/hr
- 1 IU/kg/hr
- Other: please state:
- I don't know

21. What is the commonly accepted ceiling dose of insulin used in HIET?

- 1 IU/kg/hr
- 10 IU/kg/hr
- 16 IU/kg/hr
- 22 IU/kg/hr
- I don't know

22. What is the maximum recommended inotropic infusion dose in a toxic calcium channel blocker overdose patient?

23. What are the therapeutic end-points of HIET? Tick all that apply:

- Systolic blood pressure > 90 mmHg
- Heart rate > 40 bpm
- Acidemia resolution

- Hyperglycaemia
- Urine output: 1-2 ml/kg/hr
- Improved mental status
- Persistent cardiac conduction abnormalities
- Other: please state
- I don't know

Attitude

High dose insulin euglycaemic therapy (HIET) is considered a useful treatment strategy in the management of CCB ODs. The rationale of HIET is that it reverses the cardiotoxicity in patients in several ways. Insulin is a catecholeamine-independent inotrope, improving myocardial contractility. Insulin also improves glucose uptake into cardiomyocytes, which is important as glucose is the heart's preferred energy substrate during stress. Insulin also acts as a peripheral vasodilator, reducing afterload and hence improving cardiac output. HIET should be initiated in symptomatic patients as early as possible to improve the haemodynamics of a patient as well as to help taper inotropic infusions.

24. Has the above information influenced your decision to use HIET?

1	**2**	**3**	**4**	**5**
No definitely not				**Yes definitely**

25. A patient who has taken a toxic level of calcium channel blocker presents to your ED. Despite IV fluids, calcium and inotropic infusion they remain hypotensive.
Would you start HIET on this patient?

1	**2**	**3**	**4**	**5**
No definitely not				Yes definitely

26. Have any of your colleagues used HIET?
- **No**
- **Yes:**

If yes, indicate how it influenced your decision to initiate HIET yourself?

1	**2**	**3**	**4**	**5**
Not at all influential				Extremely influential

27. Have your colleagues ever criticised you for using HIET?
- **No**
- **Yes**
- **I have not used HIET before**

If yes, did it discourage your decision to initiate HIET

1	2	3	4	5
Not at all				Very much

28. **What emotional responses (if any) do you experience when initiating a HIET? Tick all that apply:**

- **Apprehension**
- **Fear**
- **Anxiety**
- **Delight**
- **Distress**
- **Joy**
- **Other: please state**

29. **How confident are you to initiate HIET in a patient who has taken an overdose of a calcium channel blocker?**

1	2	3	4	5
Not confident				Very confident

30. **Do you feel that HIET improves patient management? If yes, please provide a short explanation for your answer.**

- **Yes**
- **No**

Explanation:

_____

31. **How likely do you think it is that doctors will consider HIET as a standard treatment?**

1	2	3	4	5
Not likely at all				Very likely

Practice

The following section relates to the practice of emergency doctors in their current ED. Please select your correct answer. There are no right or wrong answers.

32. **How do you currently manage a CCB OD in your Emergency Department?**
    - Start inotropic infusion
    - Start inotropic infusion and HIET and then refer to ICU
    - Start HIET
    - Refer immediately to ICU

- Do nothing

33. What specific vasopressor or inotrope do you prefer to initiate in a CCB OD?

- Adrenaline
- Dopamine
- Phenylephrine
- Dobutamine
- Other: Please state

34. When managing a calcium channel blocker overdose, from whom / where would you most likely seek advice?

- Internal medicine registrar
- Emergency physician consultant
- Poison centre
- A more senior doctor on the floor
- I would not seek advice
- Other: please state

35. How many patients with a calcium channel blocker overdose have you treated in the past 12 months?

Insert number

36. Have you used HIET before?

- Yes
- No

If yes, please describe any problems you encountered when using HIET.

37. Would any of the following resource limitations decrease the likelihood of your decision to start HIET? Tick all that apply:

- Unable to Call poison Centre
- Unavailable consultant for advice
- Lack of ICU beds
- CVP line confidence
- Busy emergency department
- Full resuscitation bed status
- Understaffing in the unit
- Unavailability of medications needed
- Unavailability of infusion pumps
- Other: please state:

38. Does your current work environment have the required resources and expertise to effectively implement HIET?

39. Does your past experience with treating calcium channel blocker overdoses affect your decision to initiate HIET? If so, how?

Appendix C

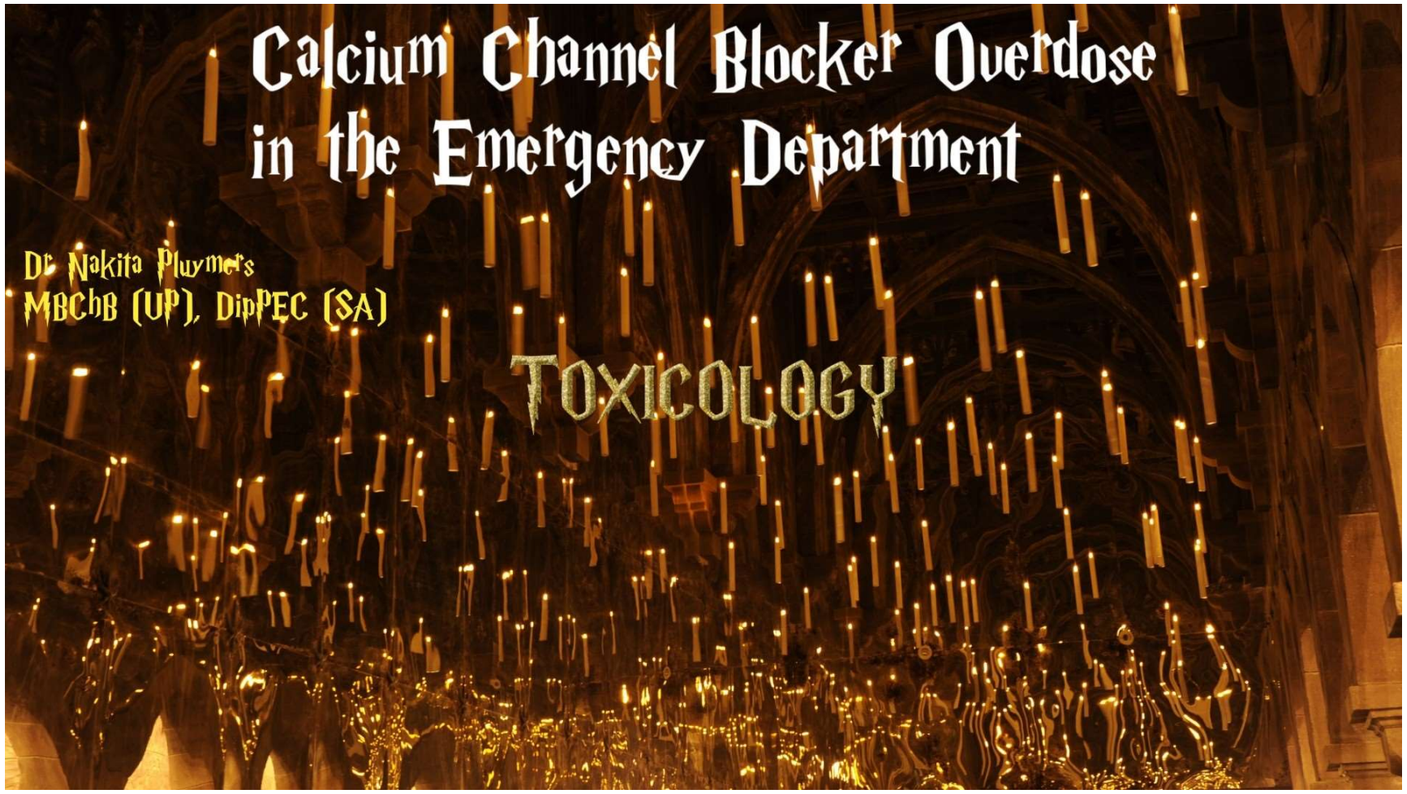
Questionnaire Mark Score Sheet: Closed-ended Questions and Open-ended questions

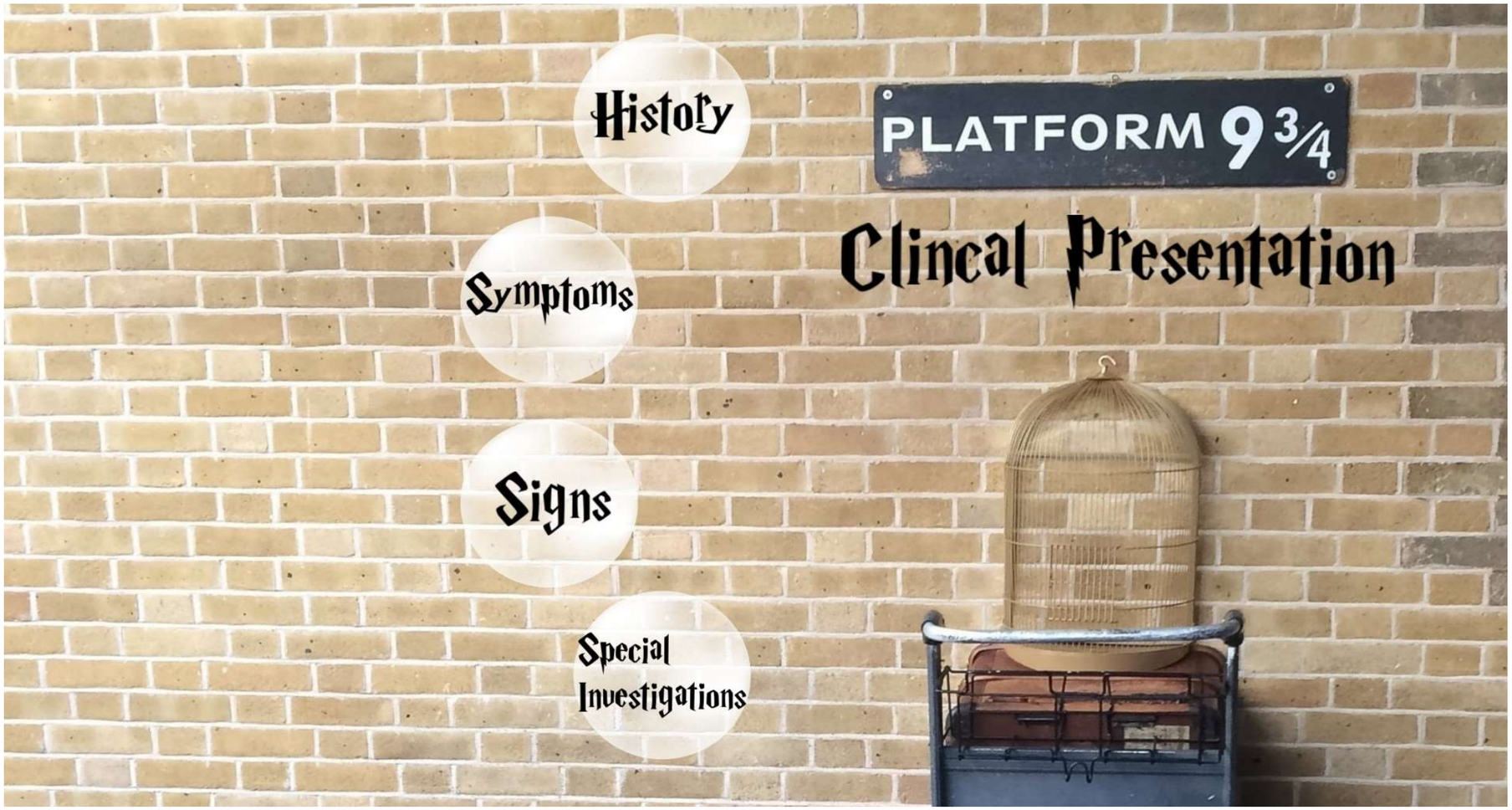
No	Answers						Marks (34)	Participants						
								1	2	3	4	5	6	7
6.	Hyperglycaemia	Hypotension	Depressed level of consciousness				(3)							
7.	20mg						(1)							
8.	Reliable IV access	Oxygenation using poly mask oxygen					(2)							
9.	Calcium Replacement	20ml/Kg IV fluid bolus	Atropine boluses: up to 3 in total	Inotropic infusion	Intubation	HIET	(6)							
10.	Increase the HIET to 5IU/Kg/hr and monitor blood pressure changes						(1)							
11.	Phosphodiesterase inhibitors	Intralipid infusion	Cardiac pacing	ECMO	Albumin haemodialysis		(5)							
12.	Glucagon has no role						(1)							
13.	20ml/Kg						(1)							
15.	High dose insulin	euglycaemia	Used in CCB toxicity	To improve myocardial contractility			(2)							
17.	Simultaneously with the adrenaline infusion						(1)							
19.	Hypoglycaemia	Hypokalaemia	Hyponatraemia	Hypomagnesia			(4)							
20.	1 IU/Kg/hr						(1)							
21.	22 IU/Kg/hr						(1)							
22.	No maximum inotropic dose because toxicology						(1)		No maximum inotropic dose					

	patient/ No ceiling dose								because toxicology patient/ No ceiling dose						
23.	SBP >90 mmHg	Acidemia resolution	Urine output 1-2 ml/kg/hr	Improved mental status			(4)								

Appendix D

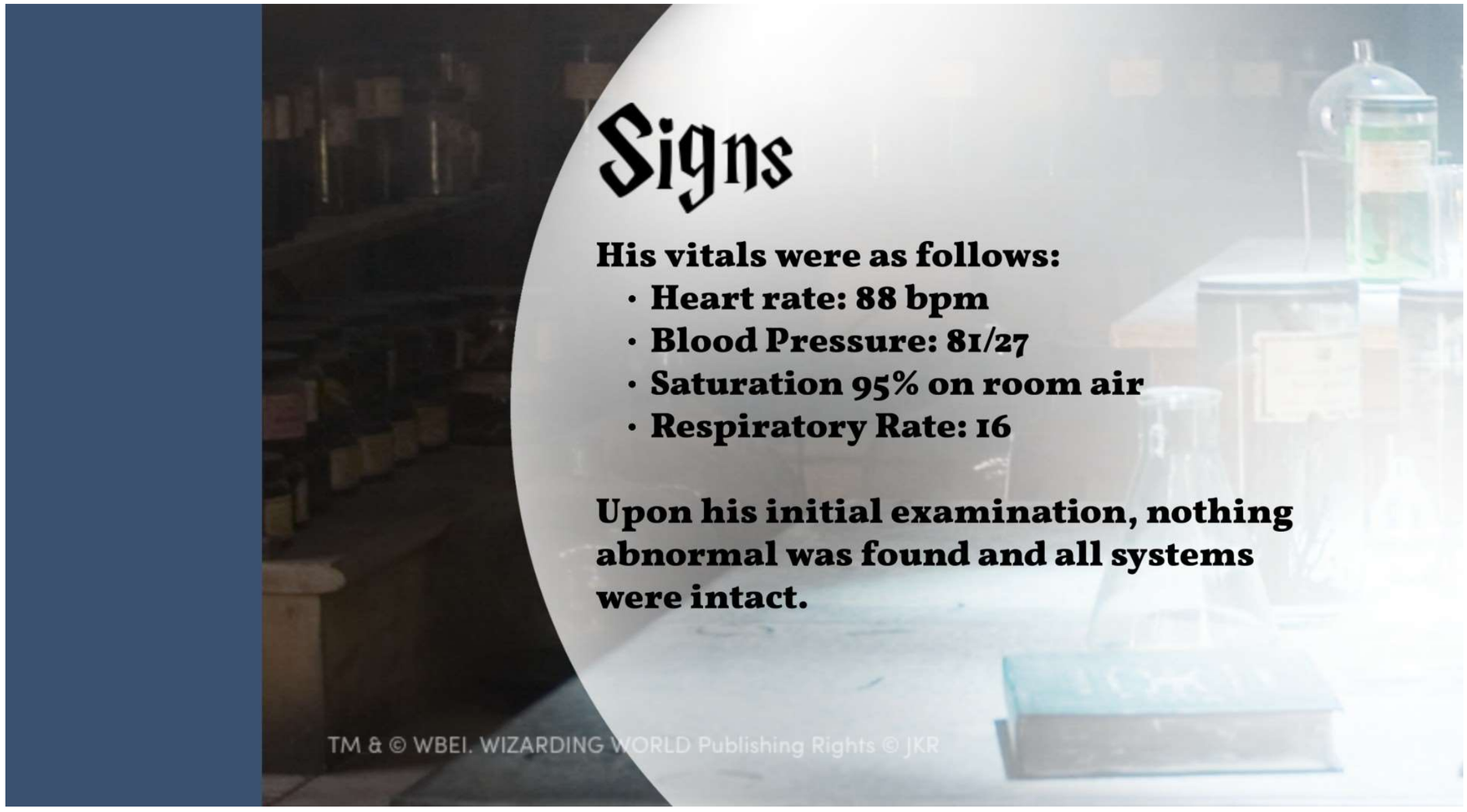
Online Webinar Presentation - https://prezi.com/v/qb9a6asztqwl/




History
Symptoms
Signs
Special Investigations
PLATFORM 9 3/4
Clincal Presentation


History
• 20yr old male
• Presented to ED at 15h30
• History of ingesting multiple tablets and mixed it with black alpirim powder at 8AM that morning
• Intentional: multiple social and personal problems


Symptoms
Now feeling:
• Dizzy
• Weak
• Lower abdominal pain


Signs
His vitals were as follows:
· Heart rate: 88 bpm
· Blood Pressure: 81/27
· Saturation 95% on room air
· Respiratory Rate: 16
Upon his initial examination, nothing abnormal was found and all systems were intact.
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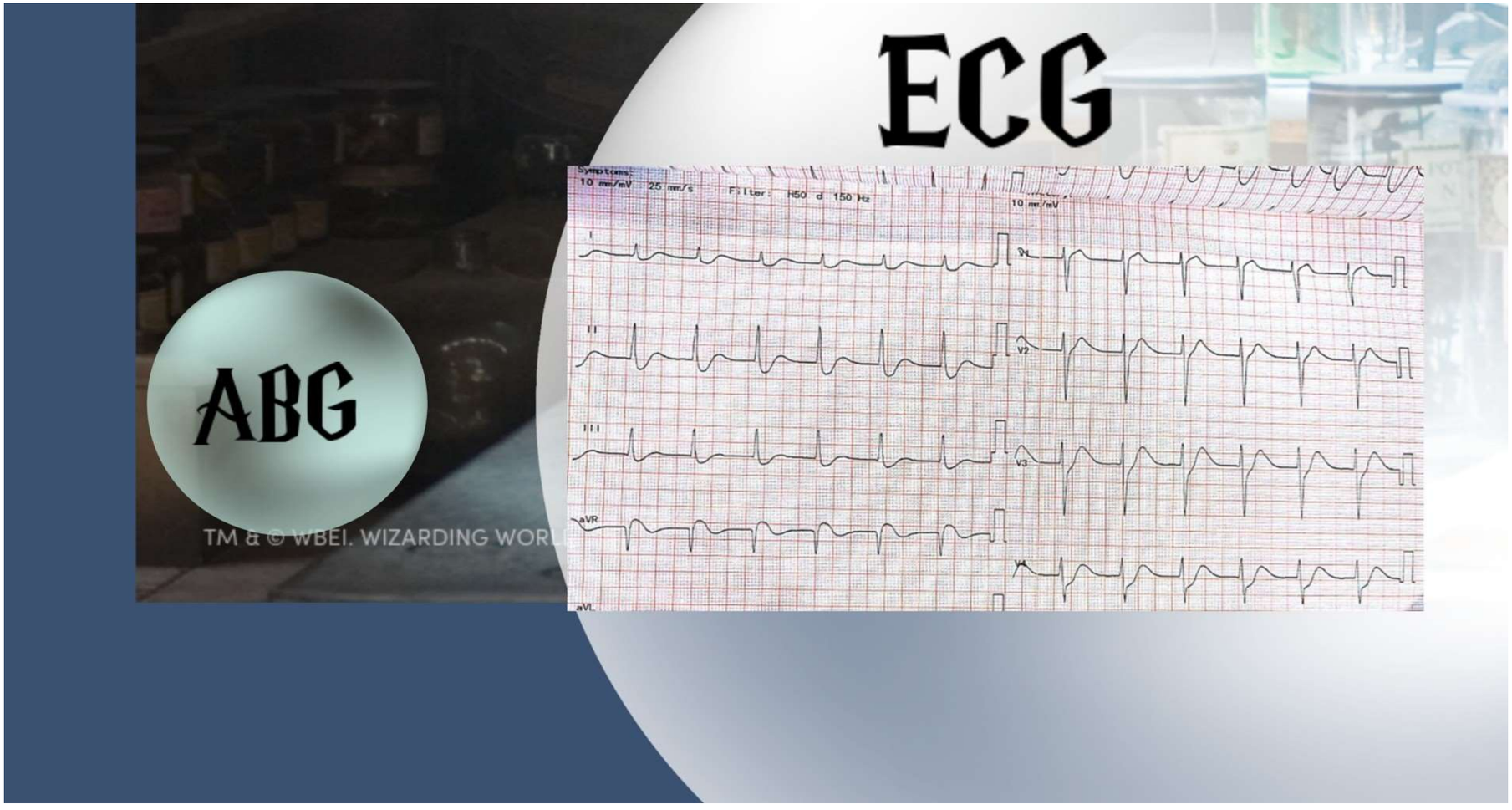
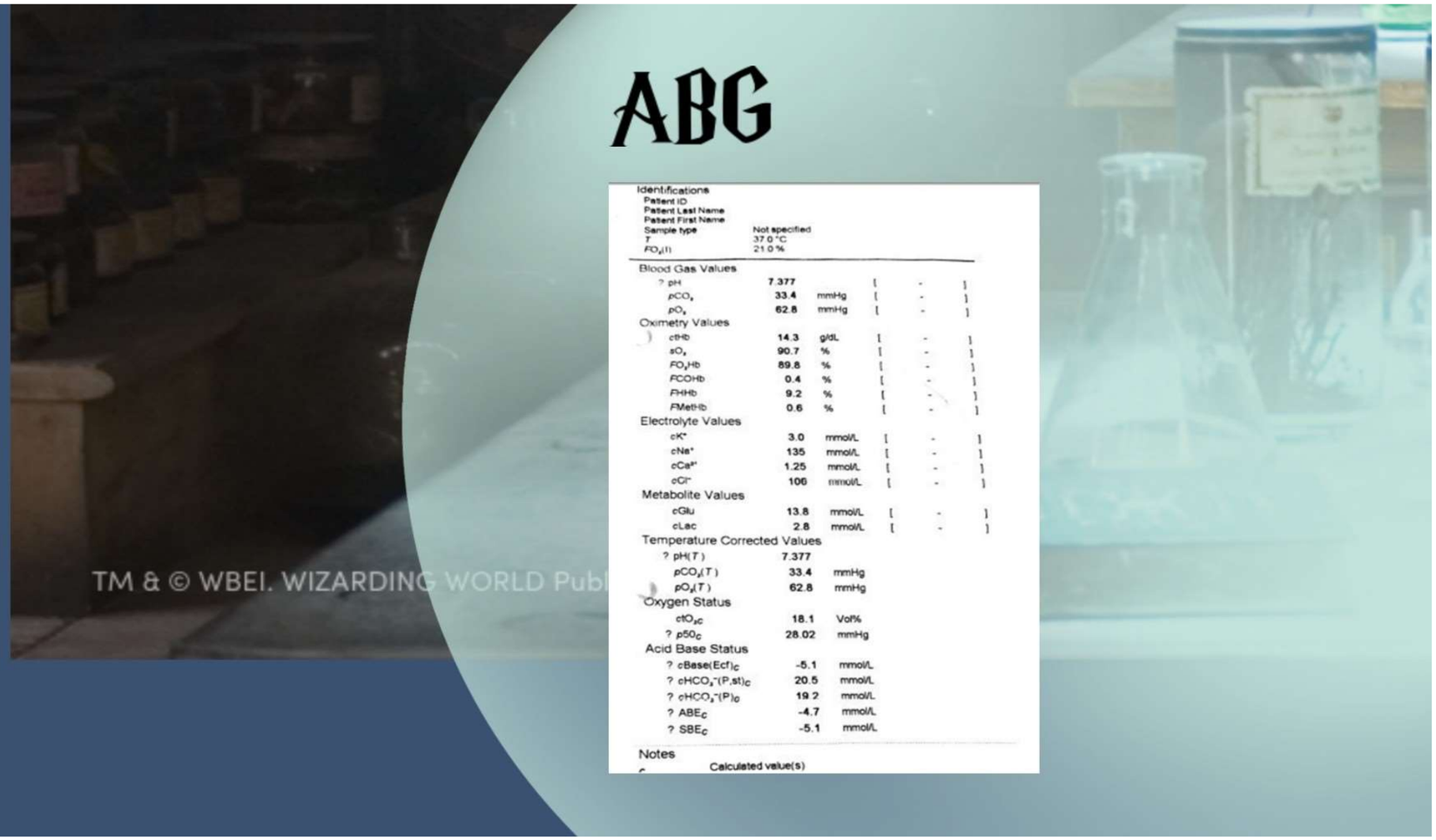
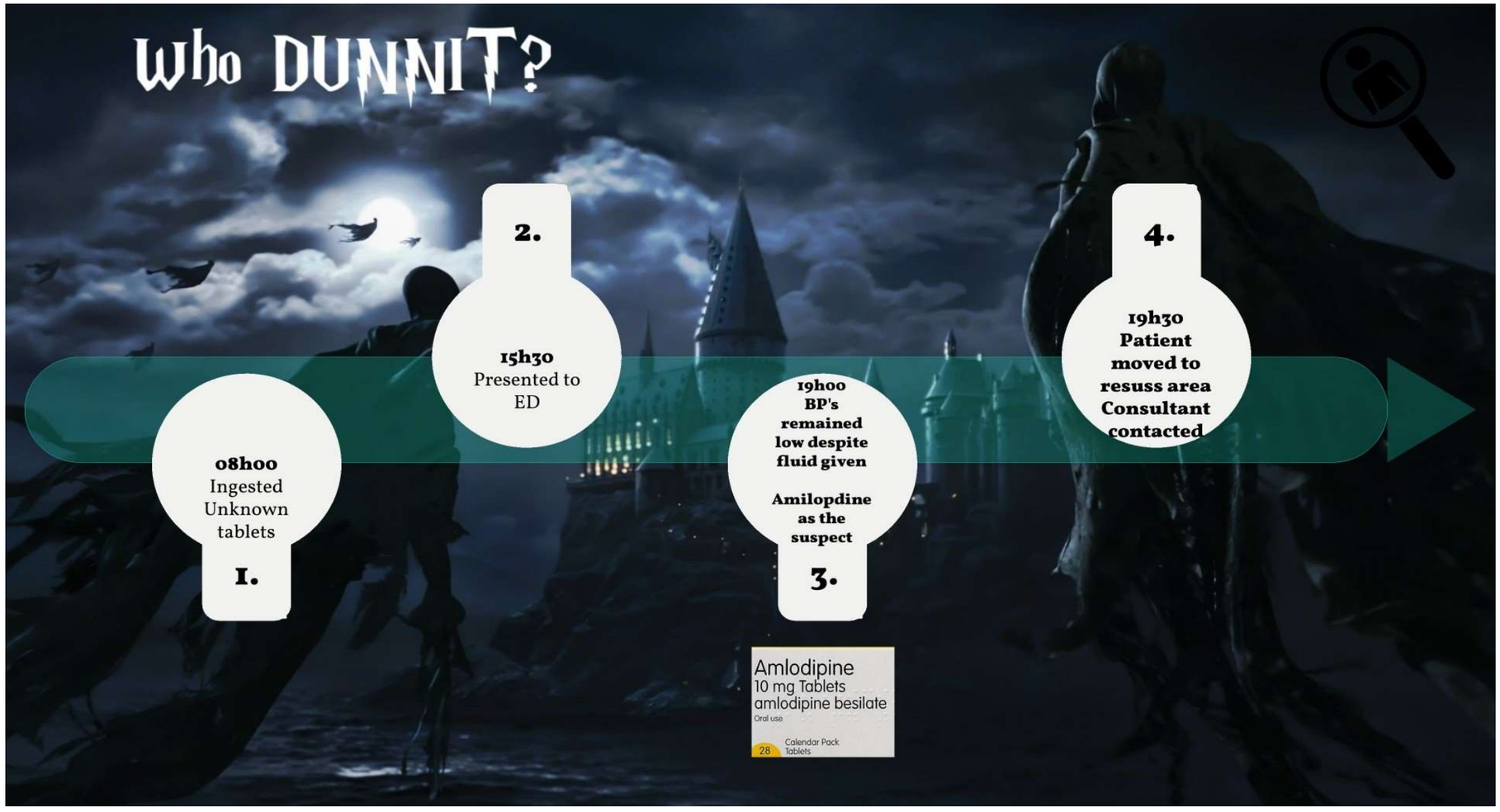

ECG
ABG
TM & © WBEI. WIZARDING WORL
Symptoms:
10 mm/mV 25 mm/s Filter: H50 d 150 Hz
10 mm/mV
I
II
III
aVR
V1
V2
V3
V4
aVL

ABG

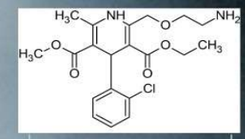


Identifications					
Patient ID					
Patient Last Name					
Patient First Name					
Sample type	Not specified				
T	37.0 °C				
$FO_2(I)$	21.0 %				
Blood Gas Values					
? pH	7.377		[	-	]
pCO_2	33.4	mmHg	[	-	]
pO_2	62.8	mmHg	[	-	]
Oximetry Values					
ctHb	14.3	g/dL	[	-	]
sO_2	90.7	%	[	-	]
FO_2Hb	89.8	%	[	-	]
FCOHb	0.4	%	[	-	]
FHHb	9.2	%	[	-	]
FMetHb	0.6	%	[	-	]
Electrolyte Values					
cK^+	3.0	mmol/L	[	-	]
cNa^+	135	mmol/L	[	-	]
cCa^{2+}	1.25	mmol/L	[	-	]
cCl^-	106	mmol/L	[	-	]
Metabolite Values					
cGlu	13.8	mmol/L	[	-	]
cLac	2.8	mmol/L	[	-	]
Temperature Corrected Values					
? pH(T)	7.377				
$pCO_2(T)$	33.4	mmHg			
$pO_2(T)$	62.8	mmHg			
Oxygen Status					
ctO_{2c}	18.1	Vol%			
? $p50_c$	28.02	mmHg			
Acid Base Status					
? $cBase(Ecf)_c$	-5.1	mmol/L			
? $cHCO_3^-(P,st)_c$	20.5	mmol/L			
? $cHCO_3^-(P)_c$	19.2	mmol/L			
? ABE_c	-4.7	mmol/L			
? SBE_c	-5.1	mmol/L			
Notes					
c	Calculated value(s)				

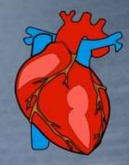

Who DUNNIT?
2.
15h30
Presented to ED
4.
19h30
Patient moved to resuss area
Consultant contacted
19h00
BP's remained low despite fluid given
Amilopdine as the suspect
3.
o8h00
Ingested Unknown tablets
1.
Amlodipine
10 mg Tablets
amlodipine besilate
Oral use
28
Calendar Pack
Tablets

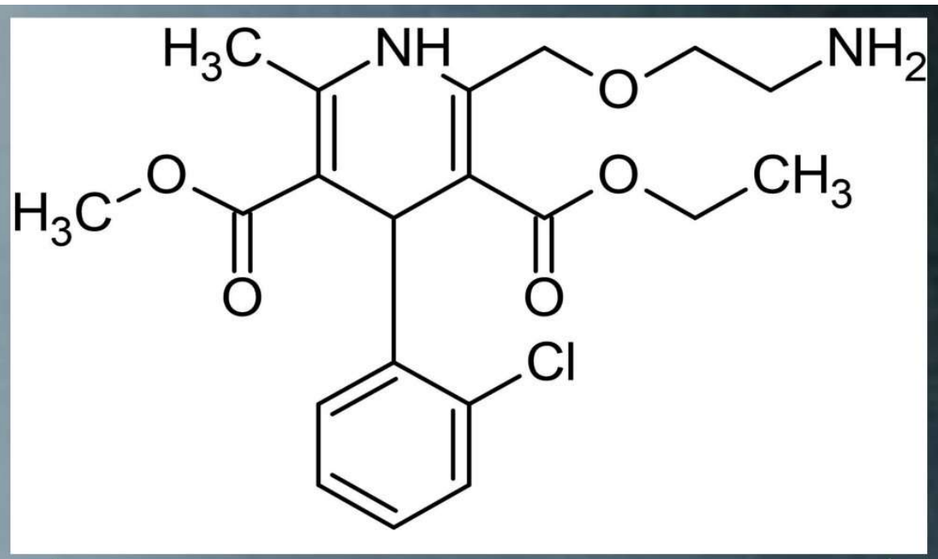
Mechanism of Toxicity

Pharmacology

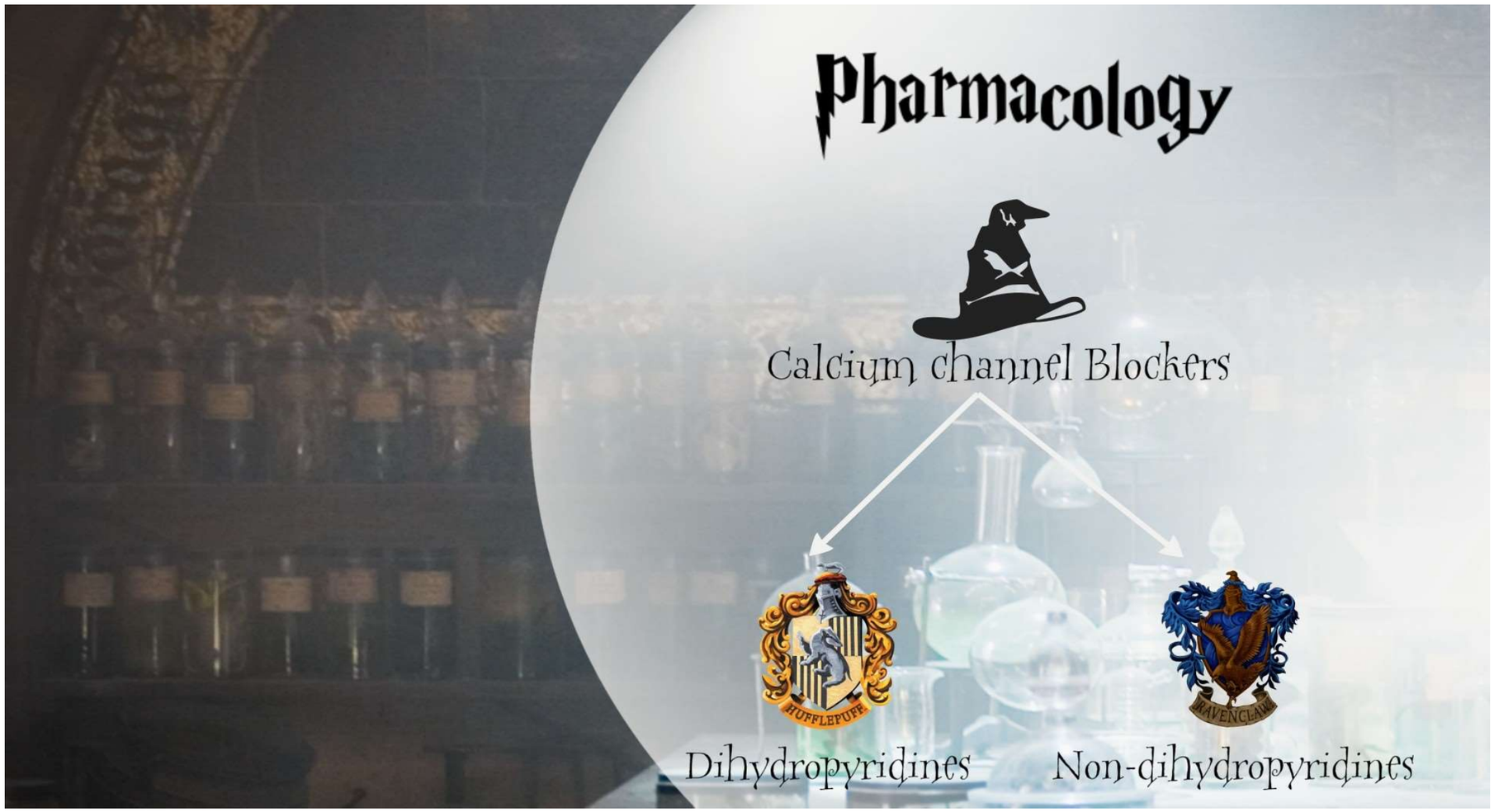


Directly antagonise the L-type calcium channels resulting in blocking calcium entry into cells: cardiomyocytes, vascular smooth muscle cells and islet beta cells

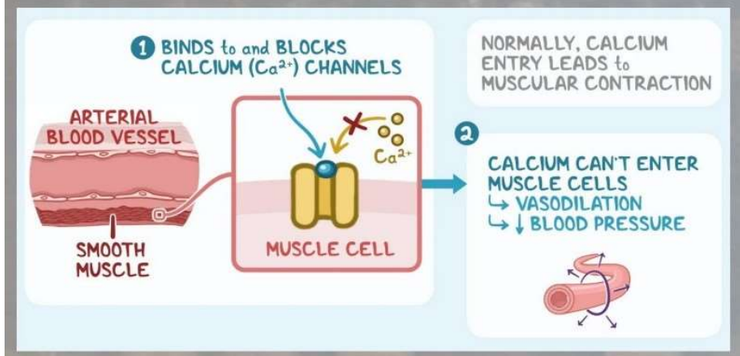




Directly antagonise the L-type calcium channels resulting in blocking calcium entry into cells: cardiomyocytes, vascular smooth muscle cells and islet beta cells


Pharmacology
Calcium channel Blockers
Dihydropyridines
Non-dihydropyridines

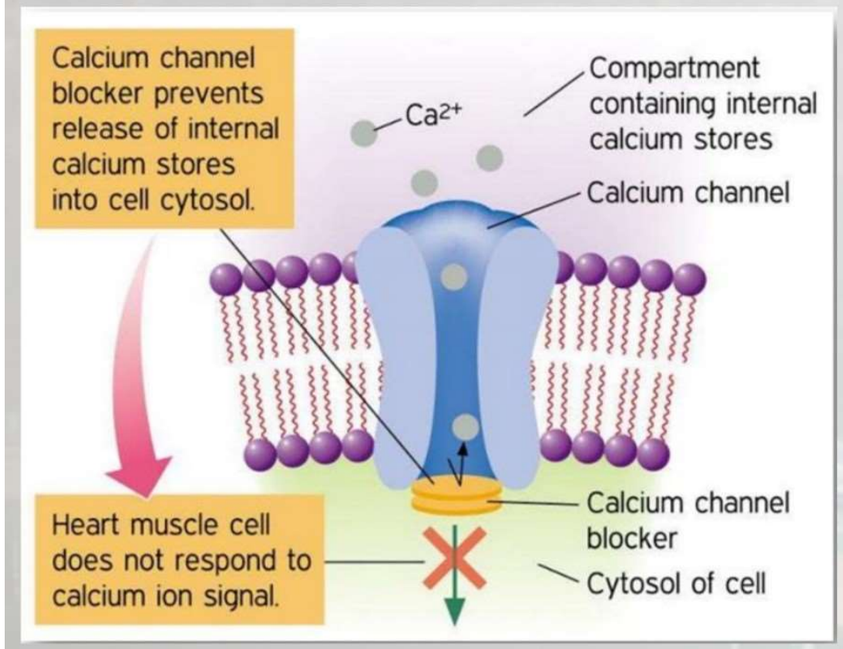
Dihydropyridines



Excellent agents for hypertension

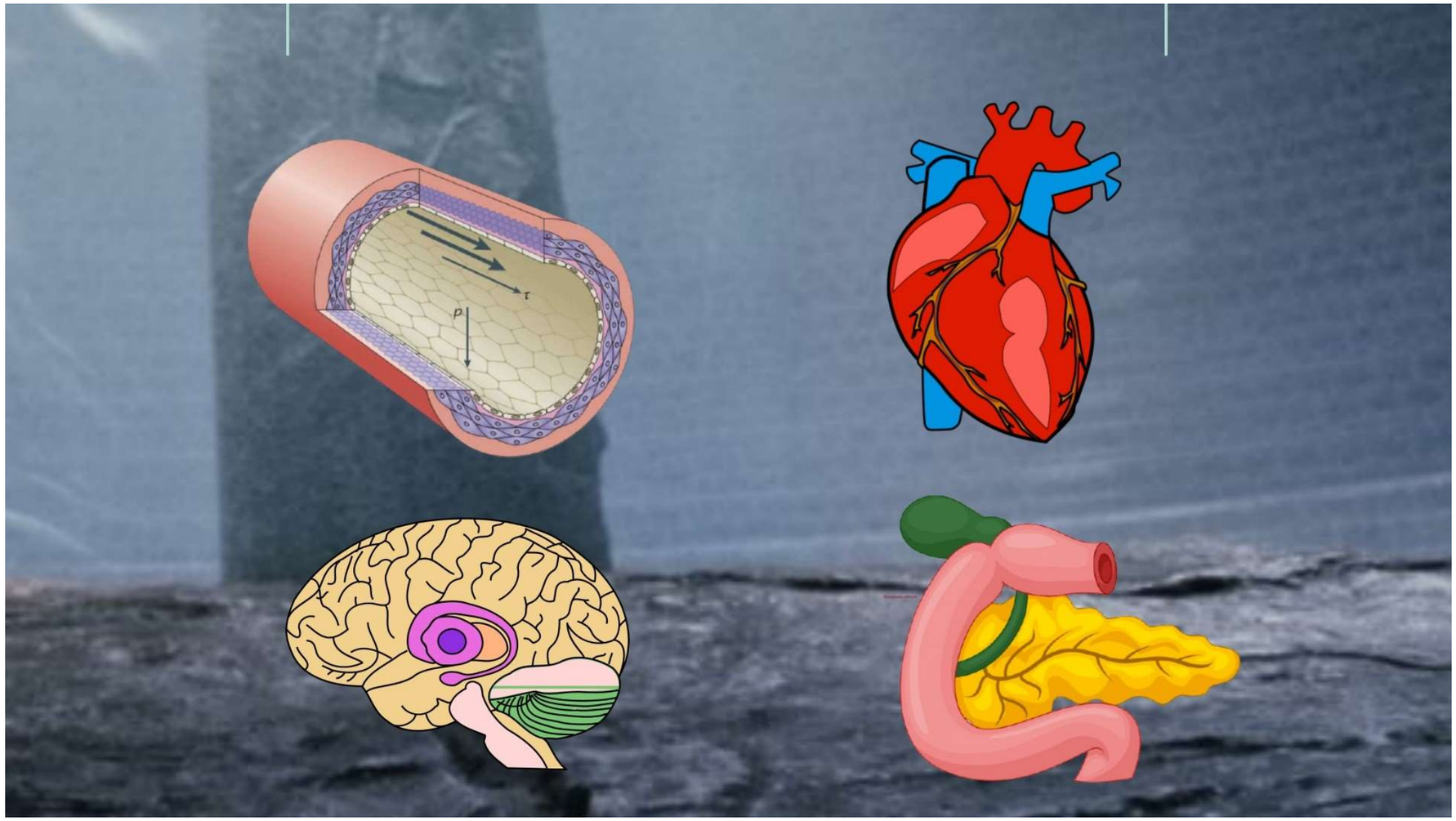
Examples: Nifedipine, Amilodipine

Non-dihydropyridines



Treat angina and arrthymias

Examples: Verapamil, Diltiazem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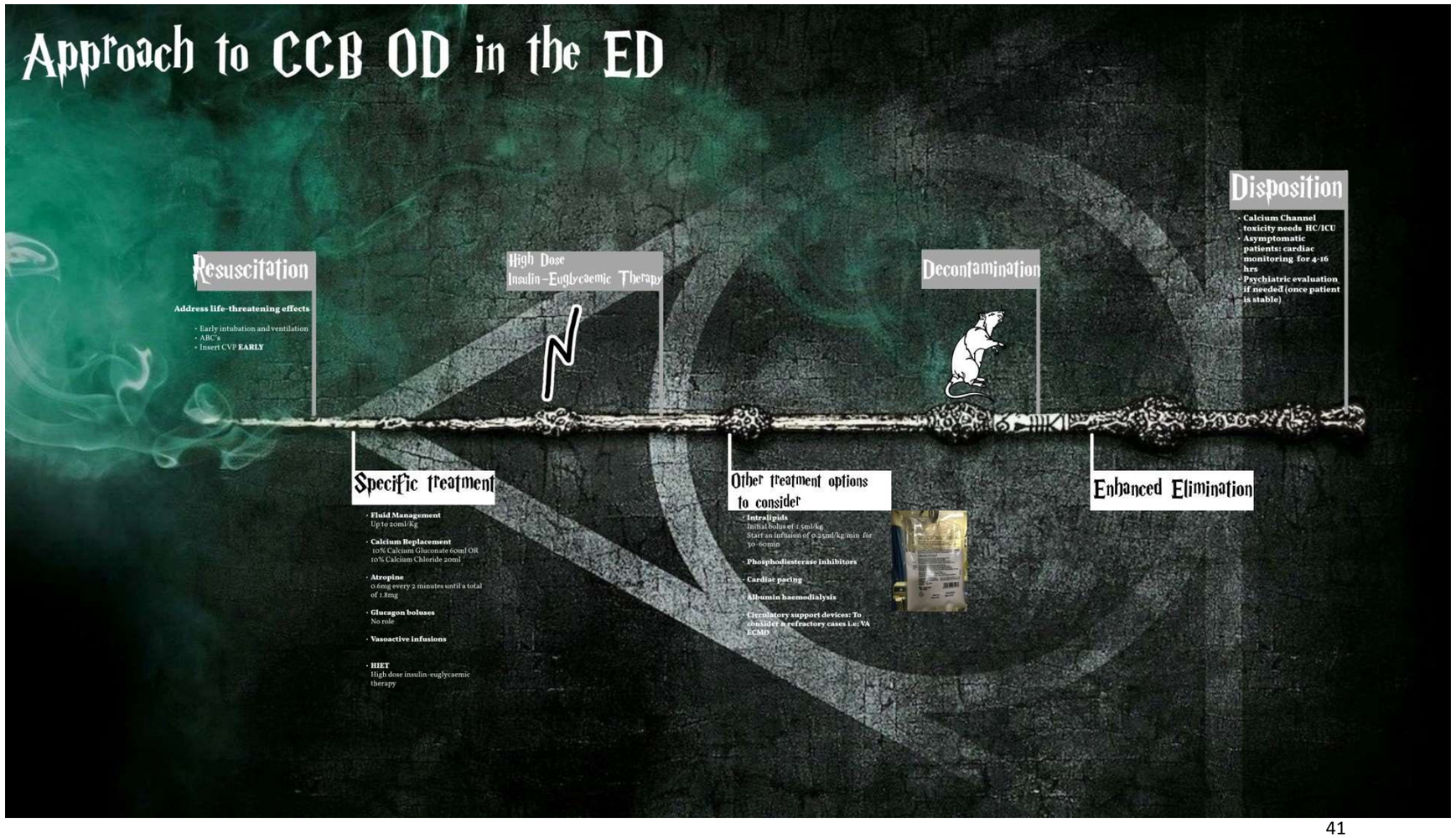
Vascular smooth muscle tone effects
• Decreased afterload
• Systemic hypotension
• Coronary vasodilation


Cardiac Toxicity Effects
• Negative inotropy: Myocardial depression
• Negative chronotropy: Sinus bradycardia
• Negative dromotropy: AV node blockade

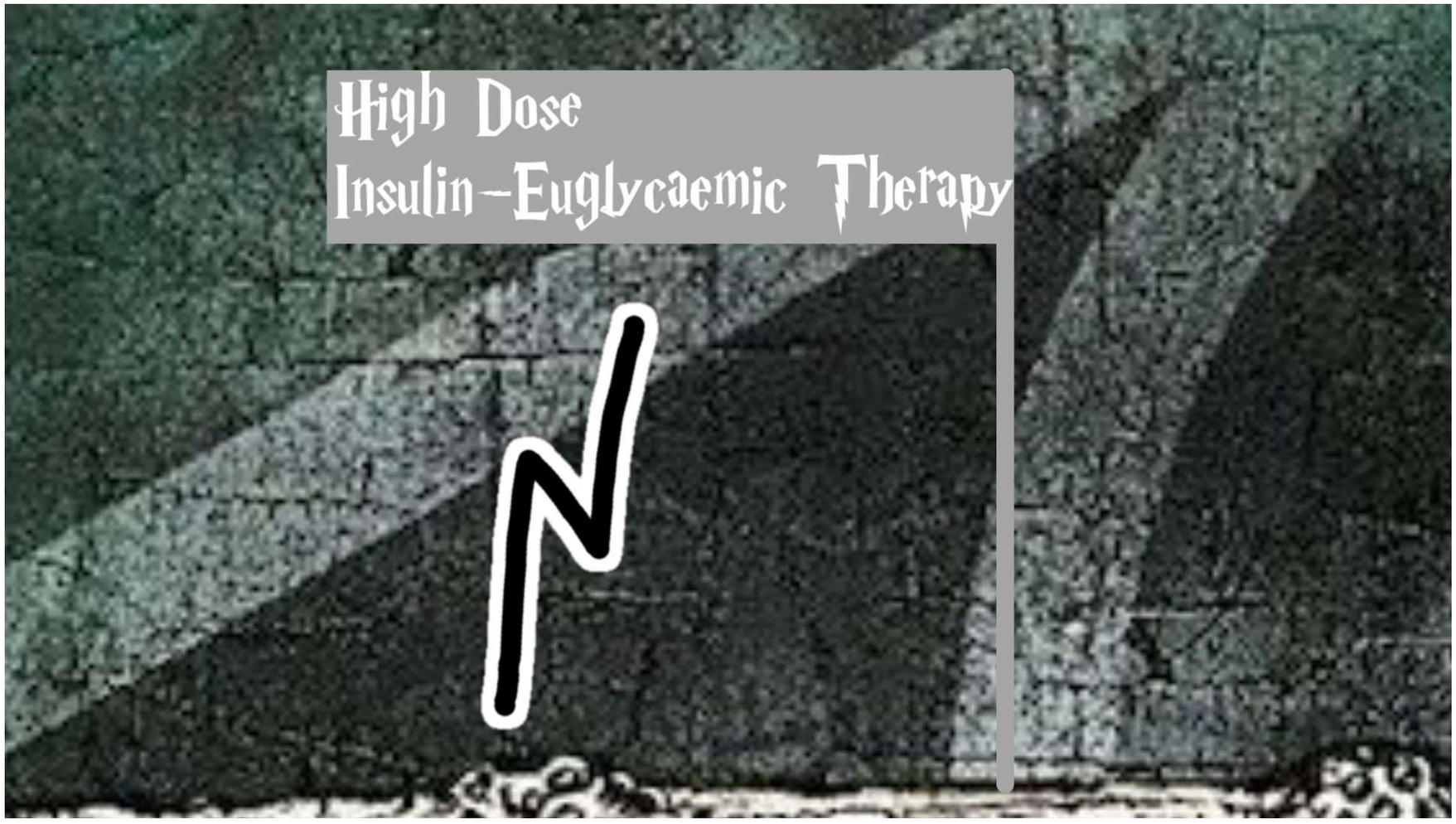

Neurological effects
• Seizures
• Coma


Metabolic effects
• Hyperglycaemia
• Hypoisulinaemia
• Impair Cardiac myocyte response


Approach to CCB OD in the ED
Resuscitation
Address life-threatening effects
• Early intubation and ventilation
• ABC's
• Insert CVP EARLY
High Dose Insulin-Euglycaemic Therapy
Decontamination
Disposition
• Calcium Channel toxicity needs HC/ICU
• Asymptomatic patients: cardiac monitoring for 4-16 hrs
• Psychiatric evaluation if needed (once patient is stable)
Specific treatment
• Fluid Management
Up to 20ml/kg
• Calcium Replacement
10% Calcium Gluconate 60ml OR 10% Calcium Chloride 20ml
• Atropine
0.6mg every 2 minutes until a total of 2.8mg
• Glucagon boluses
No role
• Vasoactive infusions
• HIET
High dose insulin-euglycaemic therapy
Other treatment options to consider
• Intralipids
Initial bolus of 1.5ml/kg
Start an infusion of 0.25ml/kg/min for 30-60min
• Phosphodiesterase inhibitors
• Cardiac pacing
• Albumin haemodialysis
• Circulatory support devices: To consider in refractory cases i.e: VA ECMO
Enhanced Elimination


Resuscitation
Address life-threatening effects
• Early intubation and ventilation
• ABC's
• Insert CVP **EARLY**


Specific treatment
• Fluid Management
Up to 20ml/Kg
• Calcium Replacement
10% Calcium Gluconate 60ml OR
10% Calcium Chloride 20ml
• Atropine
0.6mg every 2 minutes until a total of 1.8mg
• Glucagon boluses
No role
• Vasoactive infusions
• HIET
High dose insulin-euglycaemic therapy


High Dose
Insulin-Euglycaemic Therapy
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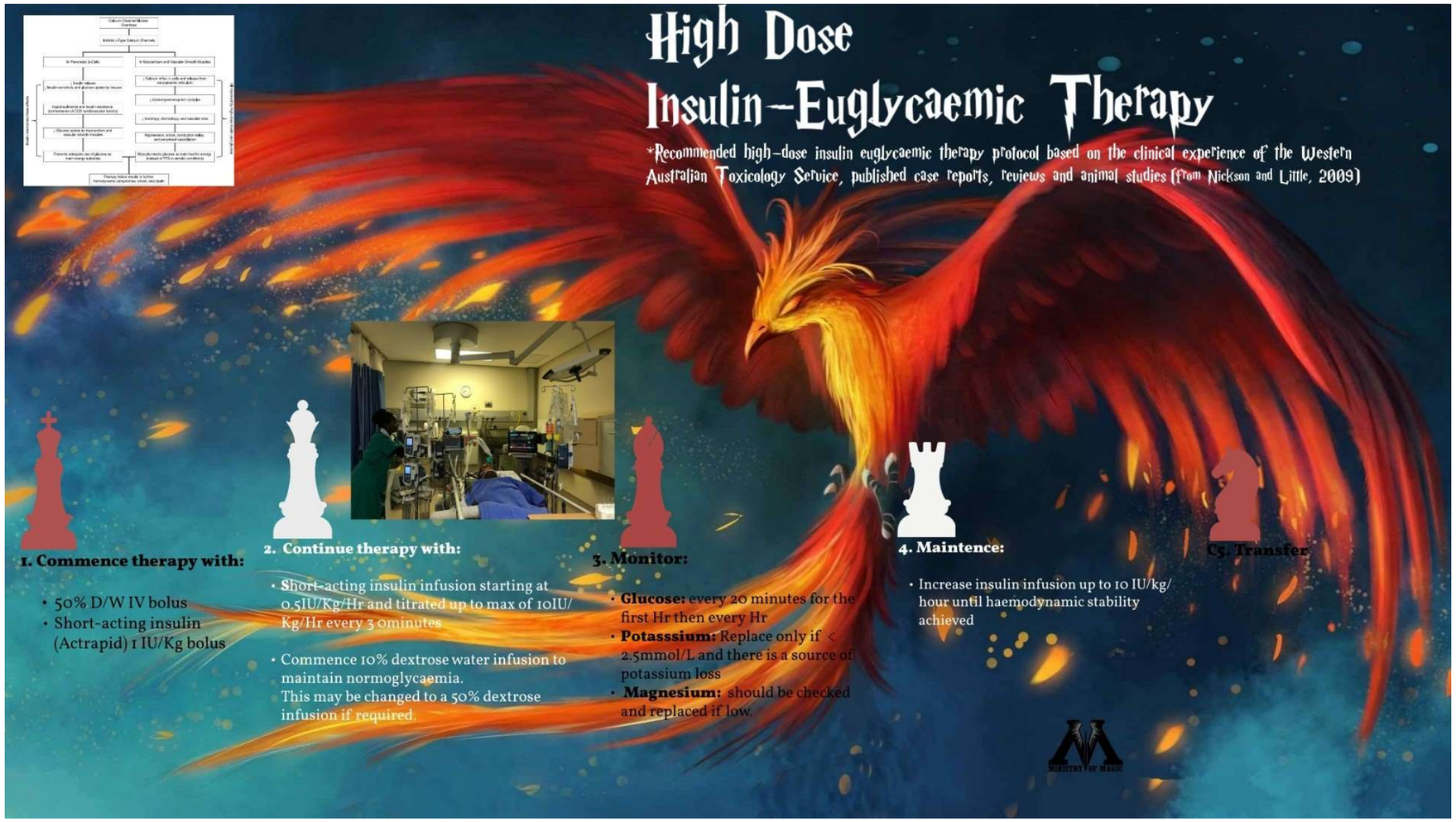
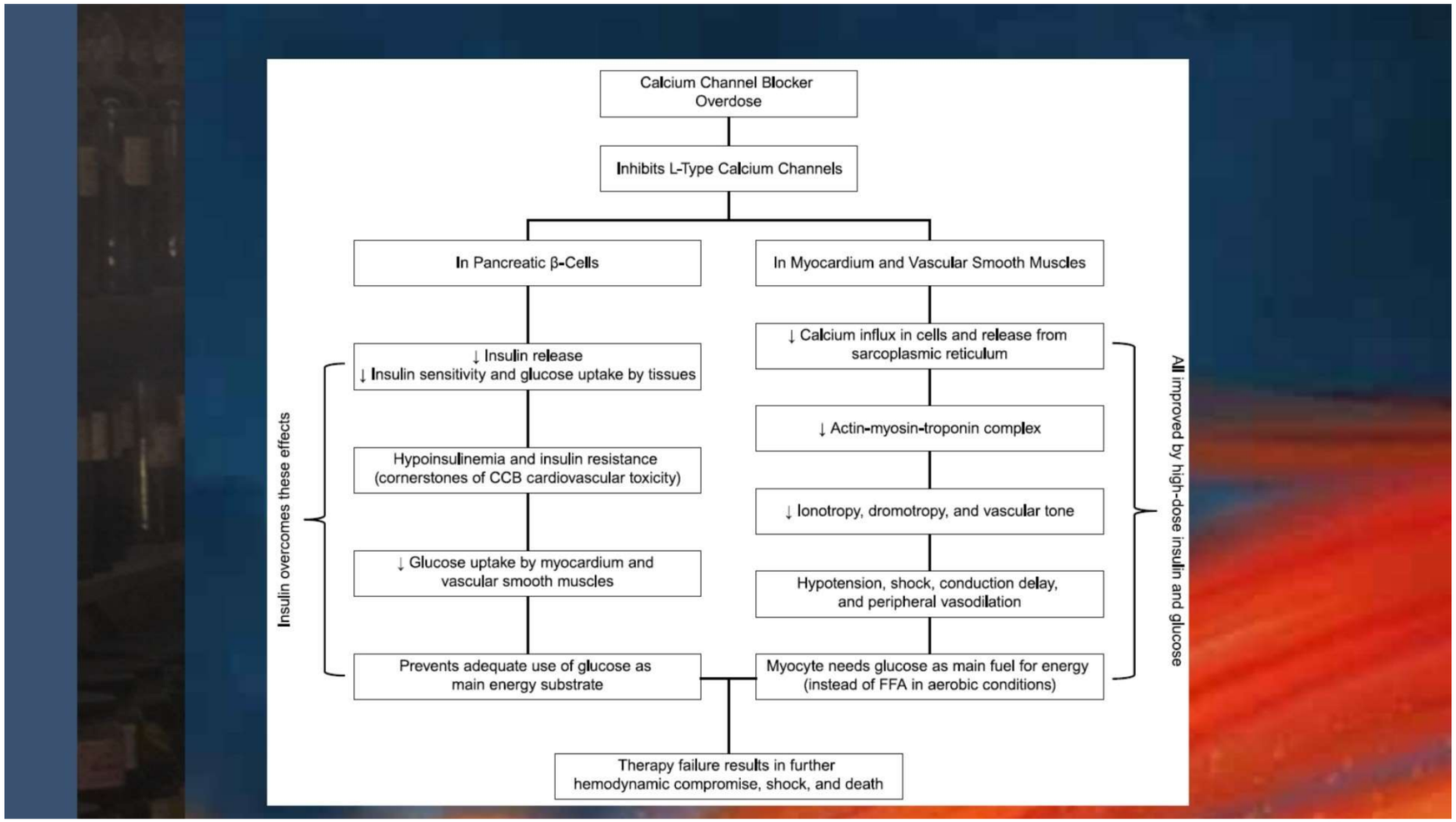
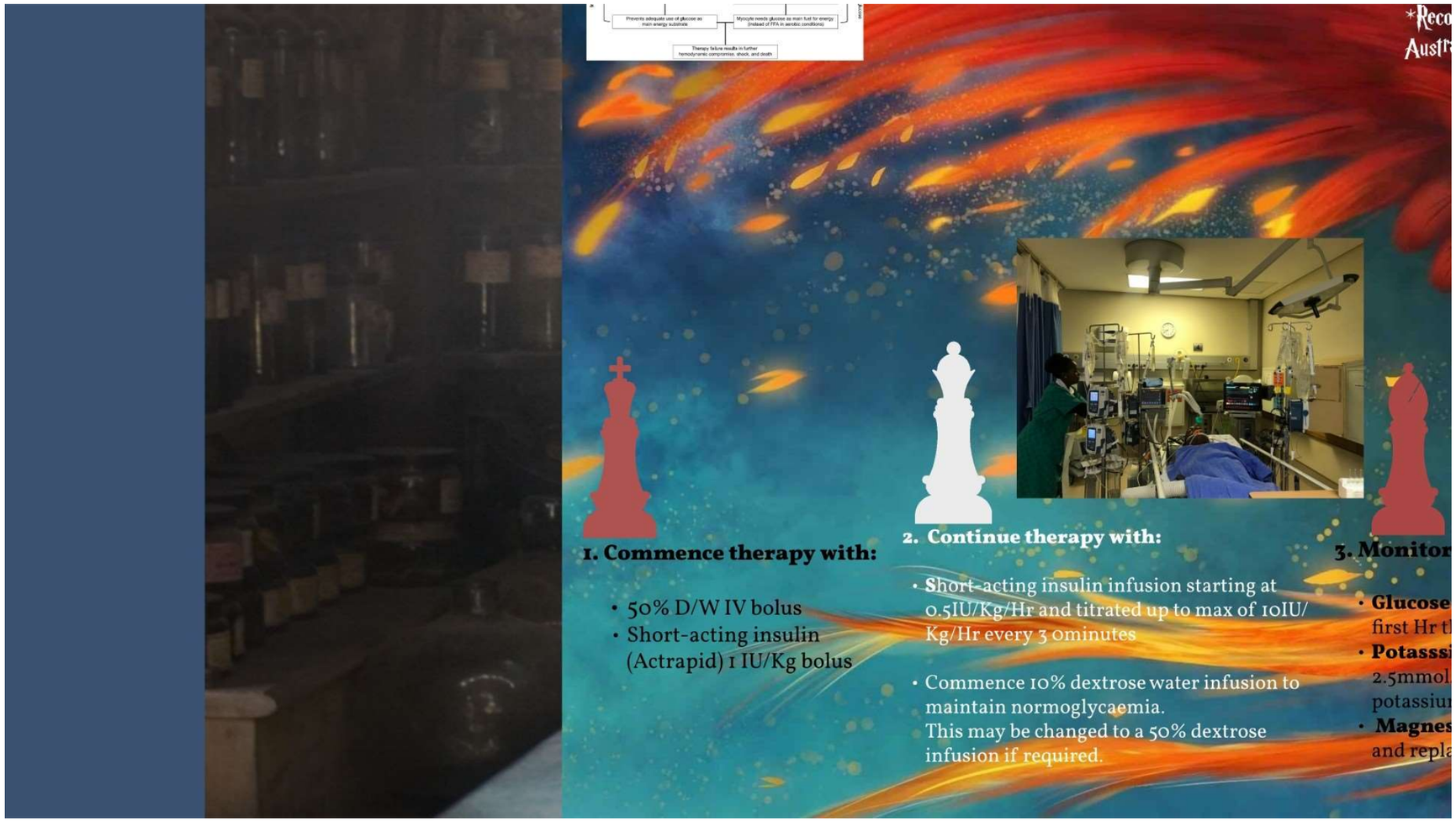
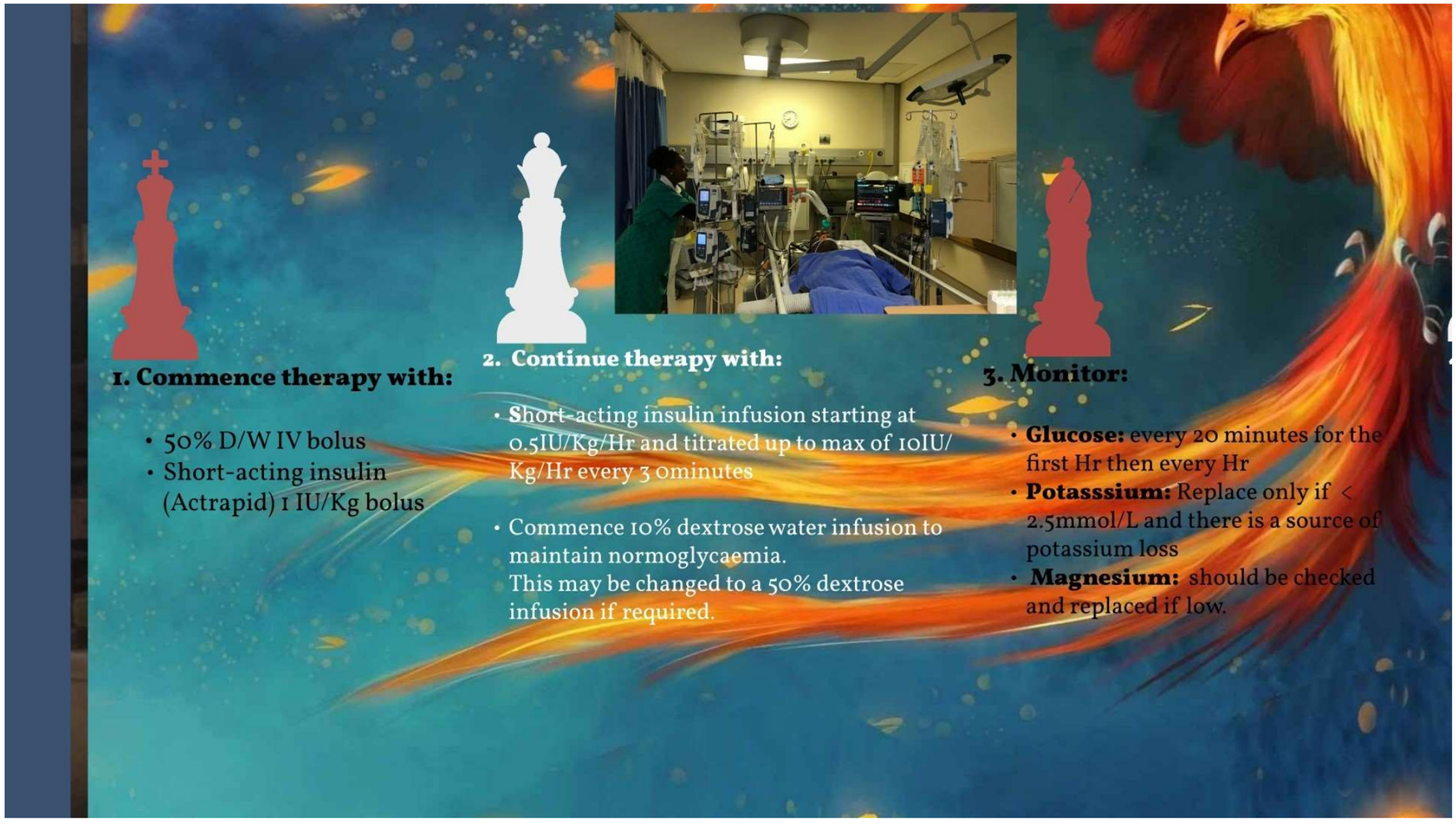

High Dose
Insulin–Euglycaemic Therapy
*Recommended high–dose insulin euglycaemic therapy protocol based on the clinical experience of the Western Australian Toxicology Service, published case reports, reviews and animal studies (from Nickson and Little, 2009)
1. Commence therapy with:
• 50% D/W IV bolus
• Short-acting insulin (Actrapid) 1 IU/Kg bolus
2. Continue therapy with:
• Short-acting insulin infusion starting at 0.5IU/Kg/Hr and titrated up to max of 10IU/Kg/Hr every 3 0minutes
• Commence 10% dextrose water infusion to maintain normoglycaemia. This may be changed to a 50% dextrose infusion if required.
3. Monitor:
• Glucose: every 20 minutes for the first Hr then every Hr
• Potasssium: Replace only if < 2.5mmol/L and there is a source of potassium loss
• Magnesium: should be checked and replaced if low.
4. Maintence:
• Increase insulin infusion up to 10 IU/kg/hour until haemodynamic stability achieved
C5. Transfer


Calcium Channel Blocker Overdose
Inhibits L-Type Calcium Channels
In Pancreatic β-Cells
In Myocardium and Vascular Smooth Muscles
↓ Insulin release
↓ Insulin sensitivity and glucose uptake by tissues
Hypoinsulinemia and insulin resistance (cornerstones of CCB cardiovascular toxicity)
↓ Glucose uptake by myocardium and vascular smooth muscles
Prevents adequate use of glucose as main energy substrate
↓ Calcium influx in cells and release from sarcoplasmic reticulum
↓ Actin-myosin-troponin complex
↓ Ionotropy, dromotropy, and vascular tone
Hypotension, shock, conduction delay, and peripheral vasodilation
Myocyte needs glucose as main fuel for energy (instead of FFA in aerobic conditions)
Therapy failure results in further hemodynamic compromise, shock, and death
Insulin overcomes these effects
All improved by high-dose insulin and glucose


Prevents adequate use of glucose as main energy substrate
Myocyte needs glucose as main fuel for energy (instead of FFA in aerobic conditions)
Therapy failure results in further hemodynamic compromise, shock, and death
1. Commence therapy with:
• 50% D/W IV bolus
• Short-acting insulin (Actrapid) 1 IU/Kg bolus
2. Continue therapy with:
• Short-acting insulin infusion starting at 0.5IU/Kg/Hr and titrated up to max of 10IU/Kg/Hr every 30minutes
• Commence 10% dextrose water infusion to maintain normoglycaemia. This may be changed to a 50% dextrose infusion if required.


1. Commence therapy with:
• 50% D/W IV bolus
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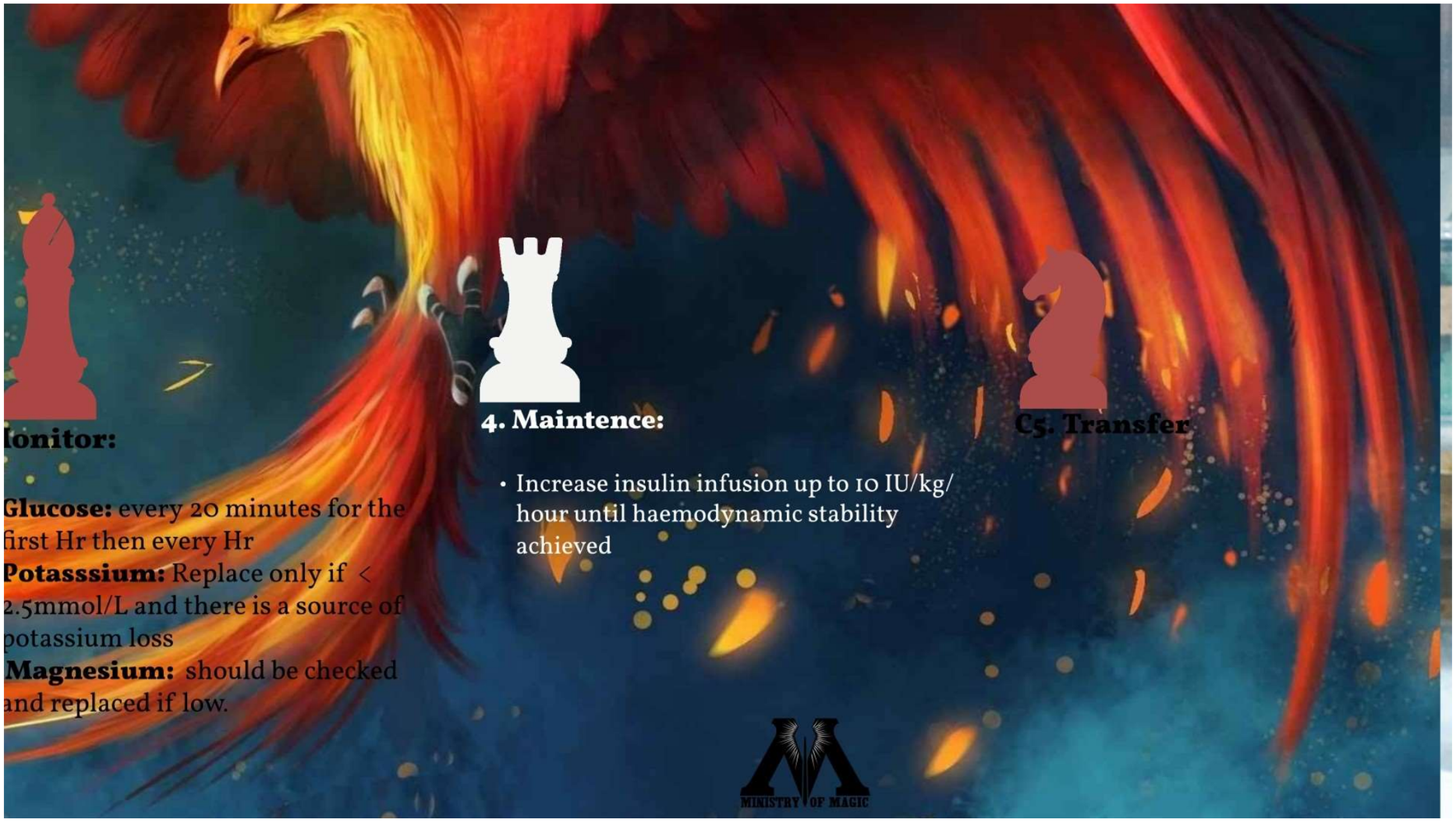
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4. Maintence:
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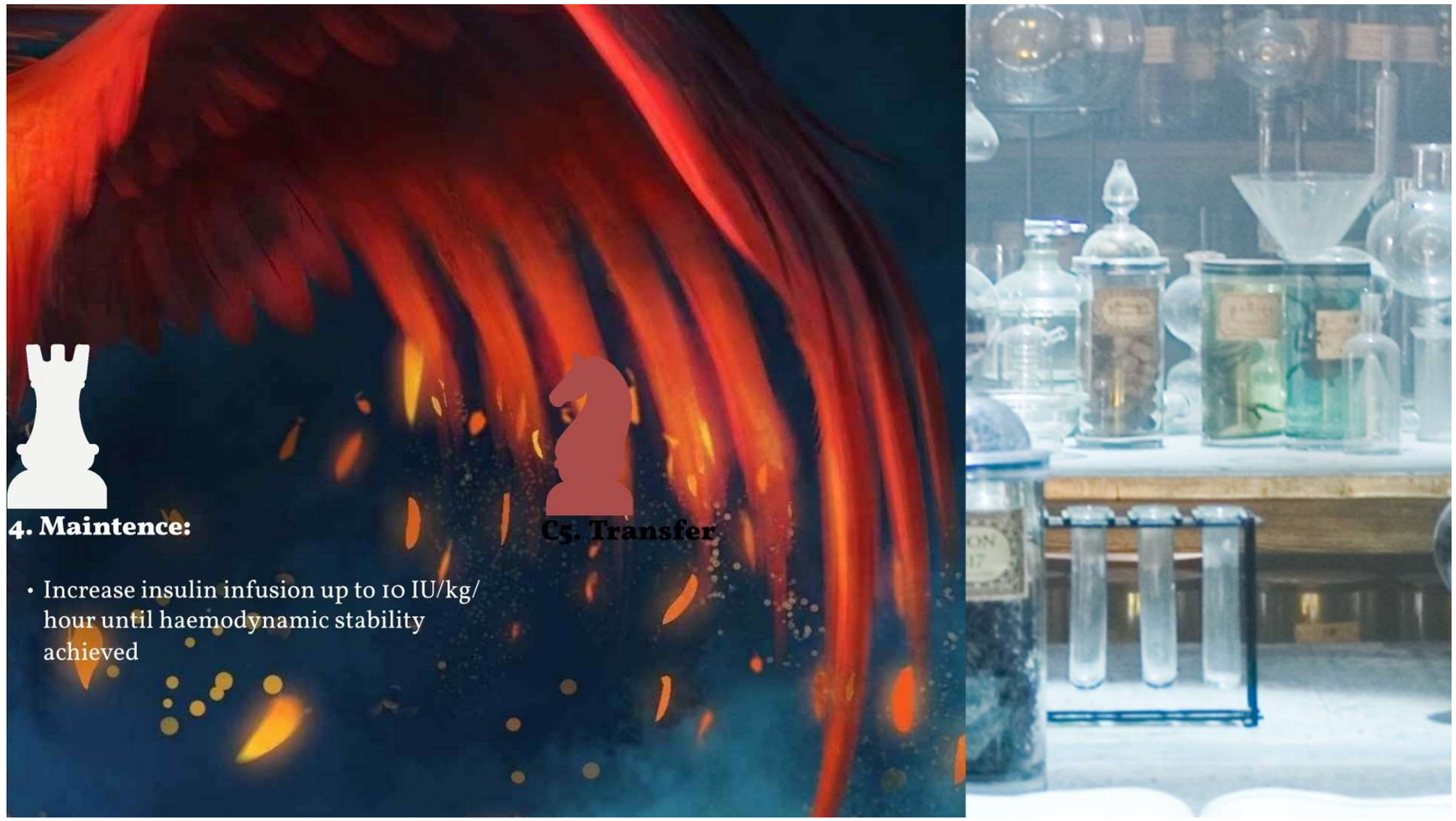
C5. Transfer
MINISTRY OF MAGIC

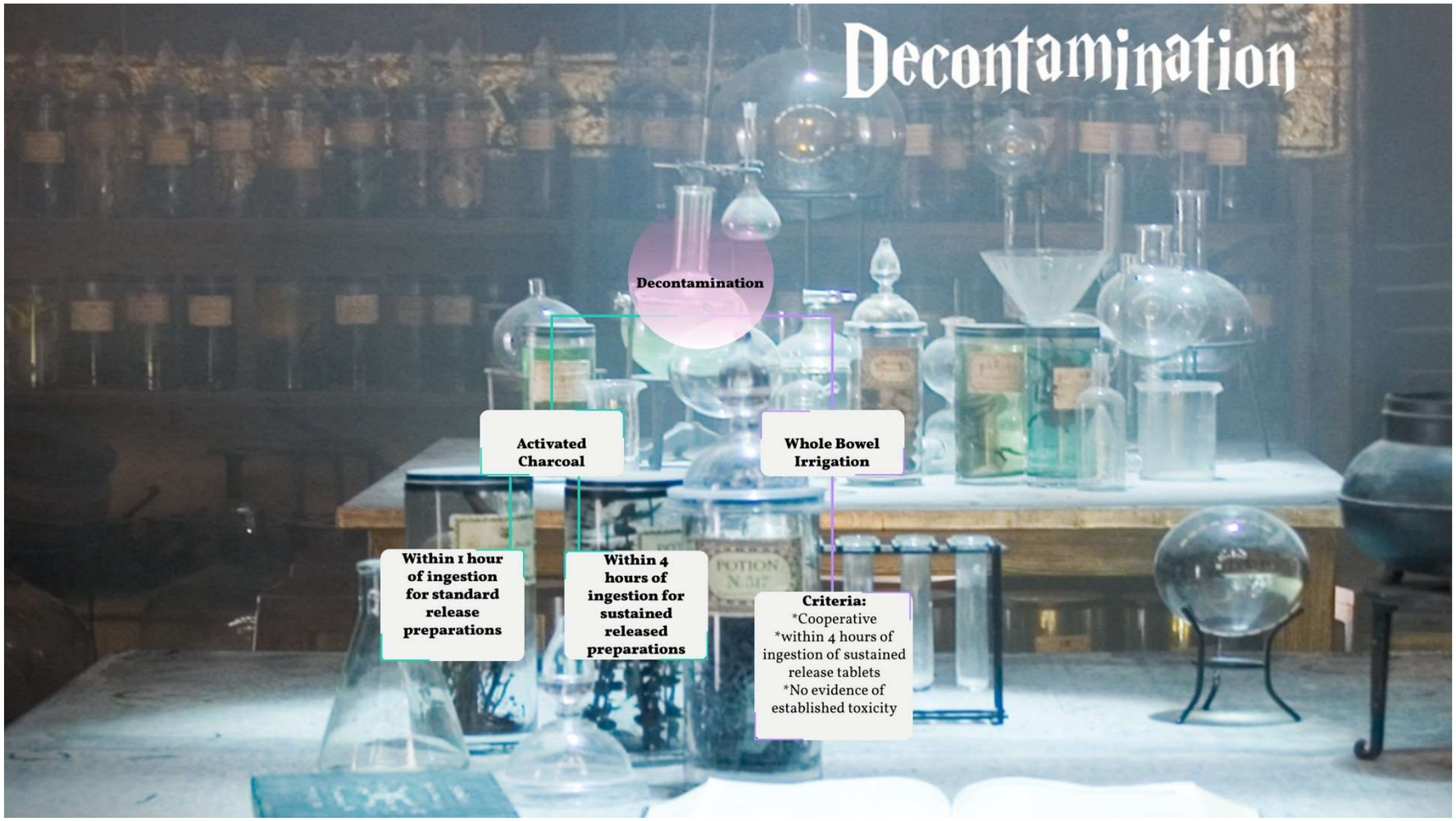

High Dose
Insulin–Euglycaemic Therapy
*Recommended high–dose insulin euglycaemic therapy protocol based on the clinical experience of the Western Australian Toxicology Service, published case reports, reviews and animal studies (from Nickson and Little, 2009)
THERAPEUTIC END POINTS
• Improvement in Myocardial ejection fraction >50%
• Improvement in BP >90mmHg SBP
• Adequate HR > 60bpm
• Resolution of acidaemia, euglycaemia
• Adequate urine output: 1-2ml/Kg/Hr
• Reversal of cardiac conduction abnormalities: QRS interval <120 ms
• Improved Mentation


4. Maintence:
• Increase insulin infusion up to 10 IU/kg/ hour until haemodynamic stability achieved
C5. Transfer

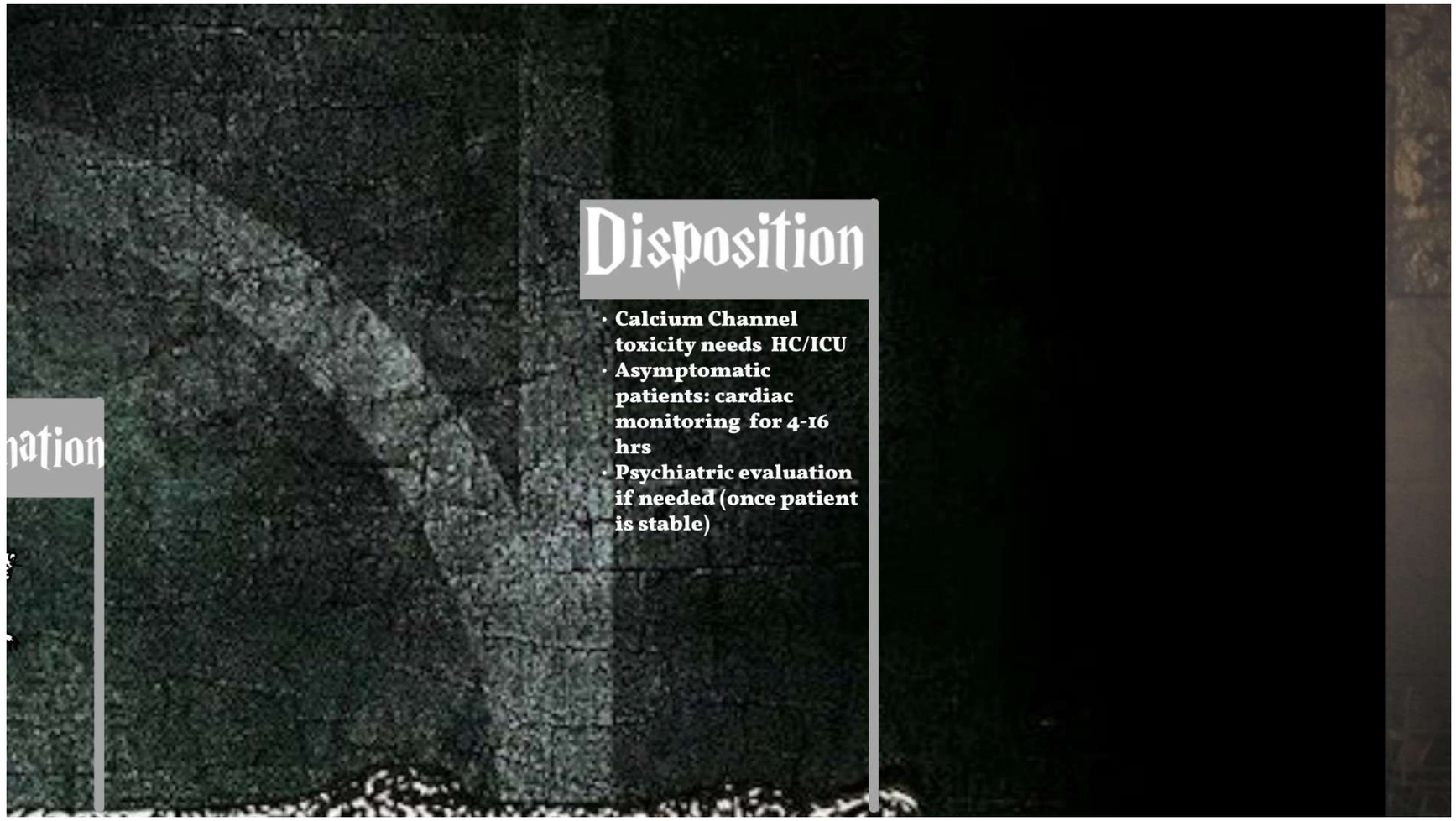
Other treatment options to consider

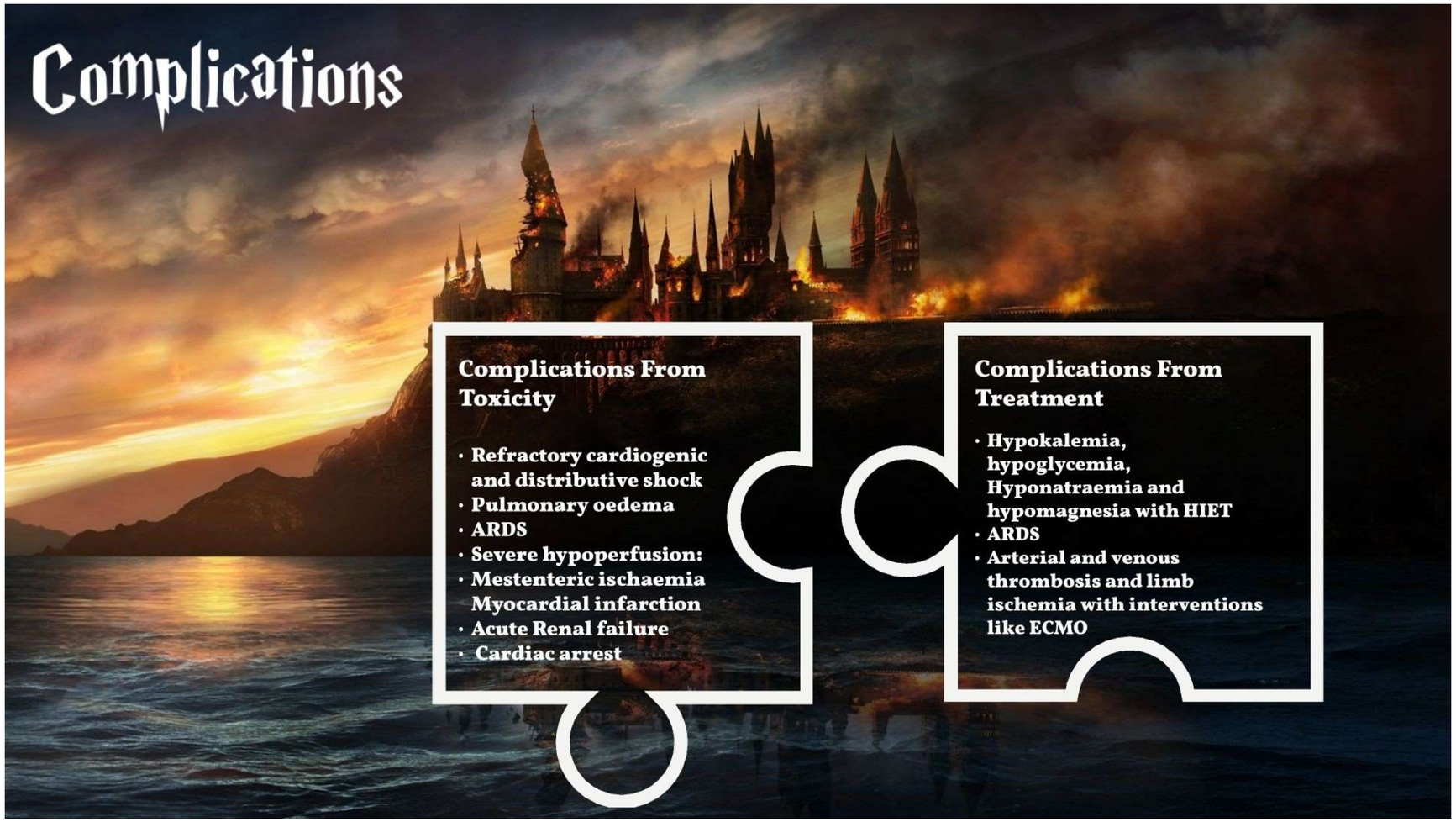
- **Intralipids**
  Initial bolus of 1.5ml/kg
  Start an infusion of 0.25ml/kg/min for 30-60min
- **Phosphodiesterase inhibitors**
- **Cardiac pacing**
- **Albumin haemodialysis**
- **Circulatory support devices: To consider n refractory cases i.e: VA ECMO**

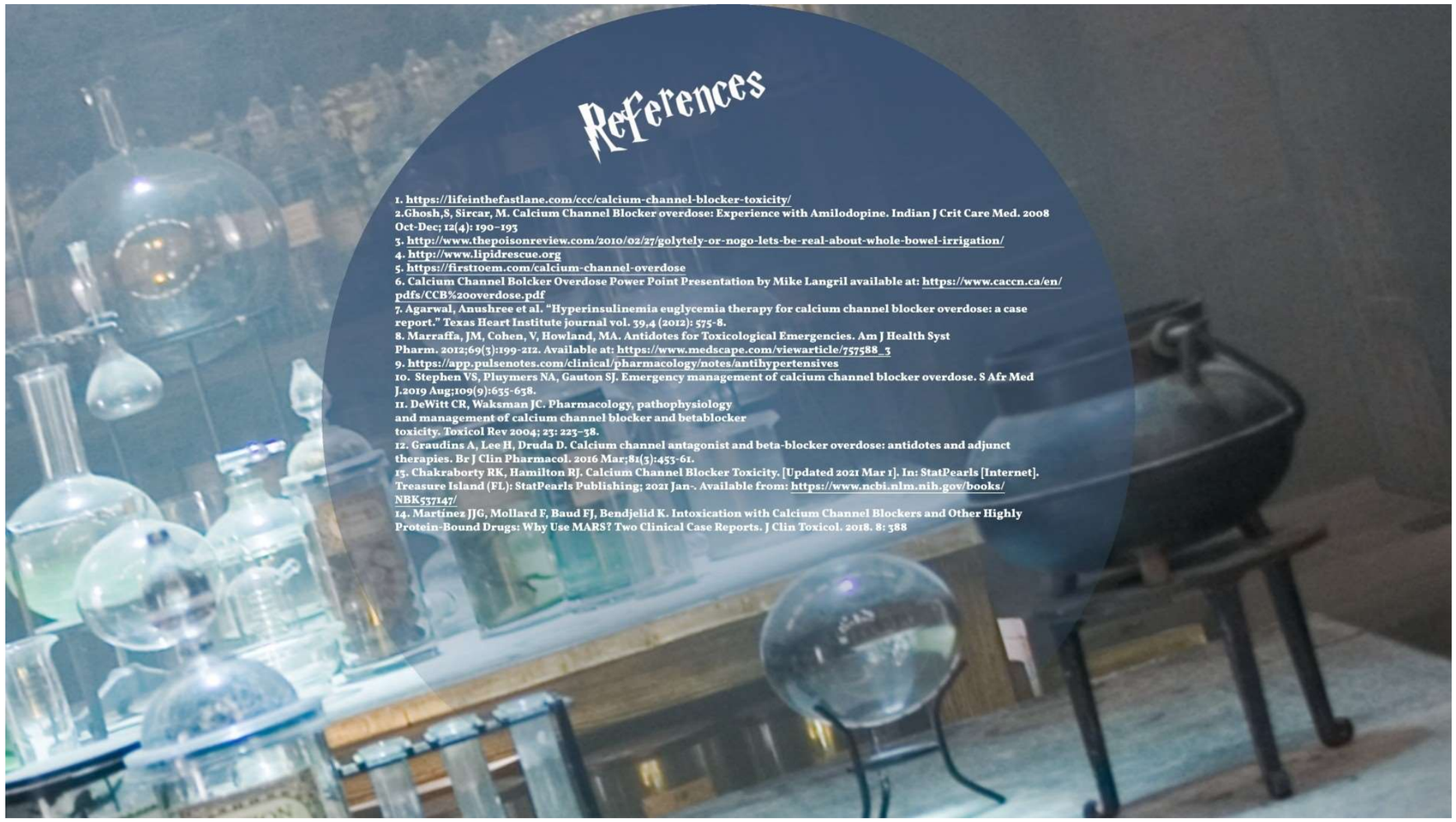

Decontamination


Decontamination
Decontamination
Activated Charcoal
Whole Bowel Irrigation
Within 1 hour of ingestion for standard release preparations
Within 4 hours of ingestion for sustained released preparations
Criteria:
*Cooperative
*within 4 hours of ingestion of sustained release tablets
*No evidence of established toxicity

Enhanced Elimination


nation
Disposition
· Calcium Channel toxicity needs HC/ICU
· Asymptomatic patients: cardiac monitoring for 4-16 hrs
· Psychiatric evaluation if needed (once patient is stable)


Complications
Complications From Toxicity
· Refractory cardiogenic and distributive shock
· Pulmonary oedema
· ARDS
· Severe hypoperfusion:
· Mestenteric ischaemia
Myocardial infarction
· Acute Renal failure
· Cardiac arrest
Complications From Treatment
· Hypokalemia, hypoglycemia, Hyponatraemia and hypomagnesia with HIET
· ARDS
· Arterial and venous thrombosis and limb ischemia with interventions like ECMO



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HOGWARTS
Dr Nakita Pluymers
MBChB (UP), DipPEC (SA)
TOXICOLOGY
PLATFORM
9 3/4
KINGS CROSS STATION
I solemnly swear
I am up to no good.
References

Final Research Protocol

The knowledge, attitude and practice of emergency department doctors in the management of calcium channel blocker overdose in South Africa

Dr Nakita Pluymers
2418919
MBCHB (Pret) Dip PEC (SA)
In fulfilment of the requirements for the degree of Master of Medicine (Emergency Medicine)

INTRODUCTION

Calcium channel blockers (CCBs) are commonly used to treat hypertension. Hypertension has a prevalence rate of 30.4% in South African (SA) adults, and CCBs are one of the recommended first-line therapeutic agents.[1] Such a high prevalence rate establishes that many patients need therapy; hence CCBs are found in many SA households. It follows, therefore, that CCBs are widely used drugs and can potentially be exploited in the form of overdose (OD).

CCBs are excellent antihypertensives, but when used in ODs, they can result in fatal consequences. Admittedly, CCB pharmacology elucidates why toxic effects occur in ODs, which causes haemodynamic instability in patients, leading to high rates of mortality and morbidity if untreated. CCB ODs are responsible for more mortalities than any other cardiovascular agent in the USA, with an estimated 42% mortality rate.[2] Clinically, haemodynamic instability is defined as perfusion failure characterised by features of circulatory shock.[3] The hallmark of CCB OD is circulatory shock caused by bradycardia, poor cardiac contractility and profound peripheral vasodilatation.[4] Therefore; emergency departments must have effective treatment therapies to prevent fatalities from CCB ODs.

The treatment of a severe CCB OD can be challenging to emergency doctors as often a multimodal therapeutic approach is needed.[5] Supportive treatments include cautious intravenous fluid administration, atropine boluses[6] or early endotracheal intubation; especially patients presenting with altered mental status due to hypoperfusion or cardiogenic shock with non-cardiogenic pulmonary oedema.[7,8] Specific treatments for CCB OD's target either calcium concentration or the increase in cyclic adenosine monophosphate concentration.[6] Intravenous calcium administration can be given; however, no haemodynamic improvement has ever been clinically proven.[5] Inotropic infusions increase cyclic adenosine monophosphate and should be initiated when patients are symptomatic with signs of cardiogenic or distributive shock.[4,5,6] Nevertheless, such therapies are not always effective in managing the cardiotoxicity of CCB OD's, and HIET (High dose insulin euglycaemic therapy) has become a well-recognised modality in these severe cases.[6]

High dose insulin euglycaemic therapy (HIET) is considered a useful treatment strategy in the management of CCB ODs.[4,5,6,9,10] The rationale of HIET is that it reverses the cardiotoxicity in patients and should be initiated in symptomatic patients as early as possible to improve the haemodynamics of a patient as well as to help taper inotropic infusions.[4,5,6,9,10] International and SA guidelines published have encouraged the use of HIET in toxic CCB OD's. An international expert consensus has a guideline to assist in the treatment of CCB OD's thereby reducing physician practice discrepancies, which have also shown improvements in cardiac output, blood pressure and possible increases in survival rates of patients.[10] Moreover, a SA clinical update of the emergency management of CCB OD[4] promulgated that HIET has become the mainstay treatment of toxic CCB OD's. Therefore, guidelines for emergency doctors exist for the early therapeutic use of HIET in toxic CCB OD patients.

It is vital in CCB toxicity that the treating physician's knowledge on how to manage, stabilise and treat such patients are well comprehended. Knowledge refers to the awareness of a condition, for example, the underlying treatment recommendations and scientific rationale.[11] This awareness of CCB toxicity will enable the clinician to follow recommendations to its therapy and help to improve patient outcomes. That being said, doctors' knowledge about the management CCB OD is linked to their attitude in this regard.

A preconceived notion towards CCB OD's and the subsequent management thereof is also of clinical importance, meaning the attitude of a doctor plays a critical role in patient management. Doctor attitudes towards managing CCB OD's can be defined as an evaluation where it is a non-tangible variable between the OD, and the response to the OD.[12] The complexity of this treatment is essential to highlight as it may have a role in defining doctor attitudes towards it. For example, treating physicians may have a negative attitude towards parasuicide patients, thereby impacting their care with undesirable results. Furthermore, reluctance from treating physicians can include lack of training and the uncertainties of therapies which could lead to poor patient outcomes.

Doctor practices are dependent upon the above two mentioned variables, namely knowledge and attitude. Without awareness and correct beliefs, on CCB OD's and the use of HIET in the initial management, the attending physician will not implement effective practices in the treatment of such patients. This denotes that the action a clinician takes in treating CCB OD's is based upon the combination of their knowledge and attitudes on this subject matter.[13] All three constituents play a role in how doctors will treat CCB OD's and affect patient outcomes.

International literature on the physician management of CCB poisoning is limited to developed countries. In Canada, only 42% of CCB OD's are managed according to the poison control centre's recommendations.[11,14] A USA study reported similar results.[15] It follows that these results are due to a lack of physician training in managing overdoses as well as limited resources, which ultimately impacts patient care.[16] Deliberate self-poisoning is a significant public health issue in developing countries[17,] and more studies need to be undertaken in SA to establish results which would improve patient care and outcomes.

In contrast, SA has no information on how doctors working in emergency departments manage CCB OD's, nor is there any research on whether HIET will be implemented in these management plans. Furthermore, there is no evidence of what specific negating or constructive influencing factors that exist. It is hypothesised that specific barriers could include a lack of physician knowledge on the toxicology and management, the fear of using such high insulin infusion doses, the unfamiliarity of using inotropes and the unknown fact that patients can initially present asymptomatic and deteriorate later. Other barriers also include the lack of resources such as multiple infusion pumps, nursing staff, and the availability of intensive care beds. A SA study done on deliberate self-poisoning cases concluded that good knowledge and awareness of health professionals on poisoning and their toxidromes would produce better patient outcomes through clinical research.[17]

Although randomised control trials (RTCs) represent the gold standard in research design, trials in deliberate self-poisoning are underpowered.[18] It follows that RCT's evaluating antidotes cannot be undertaken for ethical and legal reasons.[19,20] To assess whether doctors working in Emergency departments adhere to guidelines in the management of CCB ODs, one should consider a KAP survey. Such a survey measures the knowledge, attitude and practices of a population. It is a representative study of a specific population to collect information on what is known, believed and done concerning a topic.[21] Information gathered would be able to identify specific areas which are lacking, need improvement or implementation of protocols.[21]

Therefore, a study assessing knowledge, attitudes and practices of medical doctors in the management of calcium channel blocker overdose in the Emergency Department (ED) will be researched.

STUDY AIM AND OBJECTIVES

Study Aim: To describe the knowledge, attitudes and practices of medical doctors in the management of calcium channel blocker overdose in the Emergency Department.

Study Objectives:

1. To describe the knowledge, attitude and practices of emergency department doctors in the management of CCB overdose.
2. To describe the knowledge, attitude, and practices of ED doctors in the use of HIET in CCB overdose.
3. To describe the barriers and facilitating factors to HIET use by doctors in the Emergency Department.
4. To compare the knowledge, attitudes and practices of CCB management by medical officers working in public emergency departments, private emergency departments and Emergency medicine registrars.

METHODS

Design

The study proposed is a prospective observational cross-sectional study.

Study population and sample

1. Study site

   The survey will be solely electronic-based, using SurveyMonkey®, with an invitation email to the selected study sample. Once the survey is completed, the participants will be invited to watch an online Continuous Professional Development (CPD) accredited webinar on the management CCB OD at their discretion.

2. Study sample

The study population will be a convenience sample and will consist of the following three groups:

- Emergency Medicine registrars in the division of EM at the University of the Witwatersrand.
- Emergency Medicine doctors working in two private Emergency Departments groups: ER consulting and Nay, Wells, Hutton Piccolo Inc.
- Emergency Medicine medical officers working in Emergency Departments in State hospitals.

Inclusion criteria:

1. All Emergency department doctors willing to participate in the study.

Exclusion criteria:

1. Incomplete surveys

3. Sample Size

An estimated sample size of 90 participants will be aimed for with a breakdown of 30 participants in each group as specified in the convenience sample population.

Methods and data collection

For the methodology of the study, see appendix A, the following steps will be undertaken:

1. Identification of participants and correspondence

I will identify participants by using the following steps:

1. Division of the Emergency Medicine Wits registrars will be sent an invitation email to the survey with a link to the CPD accredited webinar. See Appendix B.

2. I will send ER Consulting Inc. and Nay, Wells, Hutton, Piccolo Inc. practice consultants an informal email with information on the survey and the CPD accredited webinar to send to their staff members. See Appendix C.
3. I will also send an informal email with information on the survey, and the CPD accredited webinar to send to state-employed medical officers. See Appendix C.
4. For both convenience samples in private and public ED's, I will also advertise the survey with the CPD accredited webinar on social media for such doctors to partake. See appendix C.
5. The study population consisting of the private practice ED's will be identified by those doctors responding to the informal email sent by their practice manager, by clicking on the link to the online survey.
6. The study population consisting of the state ED's will be identified by those doctors responding to the informal email sent to them, by clicking on the link to the online survey.
7. The study population which will respond to the social media advert will be identified as those clicking on the link to the online survey.
8. The invitation email will be sent to prospective participants outlining the survey. This email will describe who the researchers are, the University they are affiliated to, the purpose and aim of the research, how long the survey will take and the online survey link as the body of the email.
9. If the responses from the above methodology did not receive an adequate response for the estimated study sample size, a second round of identification will be done. I will go in person to both state and private emergency departments and invite interested medical officers to complete the survey. I will explain to prospective participants what the survey is about and how their responses will be anonymous and not be shared with neither their employers nor any other external parties. I will explain that participation is purely voluntary, and they have the right to withdraw or refuse participation at any stage. The participant may choose to either complete the survey on a tablet that I will provide or if they would prefer to use their own electronic device, I would send them the survey link via a message in order for them to complete it on their phones or they could scan the QR code I would provide.

3. The survey

1. I will ensure the online survey link will be included in the invitation email. This online survey will be hosted by SurveyMonkey®, which is an online software and questionnaire tool, which will be self-administered.
2. During the analysis of the survey, I will ensure that all the responses will always remain anonymous by not capturing personal data in the survey.
3. Informed consent will be assumed by participants if they complete the survey.
4. The survey will be designed in such a way that participants will be prevented from going back to previous questions and editing their responses on those questions.
5. It will contain a combination of open, closed and case-based multiple-choice questions as adapted from *Brassard et al.*, see appendix D. It is important to note that the *Brassard et al* questionnaire was a semi-structured interview of specialist intensivists with the purpose of identifying barriers and facilitators to adherence to poison control centre recommendations for CCB intoxication.[11] The questionnaire has been adapted and is now self-administered with the purpose of identifying emergency doctors' knowledge, attitude and practices in managing patients with a CCB overdose. The breakdown is as follows:
    1-5: demographics
    6- 23: knowledge
    24-31: attitudes
    32-39: practices

4. Webinar on CCB OD management

1. Once the survey has been completed, the participant will receive an automated thank-you email which will contain the webinar link to view at their discretion.
2. I will host a pre-recorded webinar using Prezi® to educate participants in the emergency management of CCB OD in the emergency department. The webinar will focus on a case study based on a patient presentation and will highlight the pathophysiology, toxicodynamics, general management and specific management of a CCB OD lasting about 40 minutes in total.

5. CPD accreditation

There will be an optional CPD accreditation by Wits DEM once the webinar has been completed if participants wish to provide credentials and personal information. The anonymity of the survey will remain as this will occur after the survey has been taken.

Variables

Dependent variables will be knowledge, attitude and practices. In contrast, the independent variables include where the emergency doctors work, either in the state, private practice or specialising as an emergency medicine registrar, the doctor's level of experience and their exposure to CCB OD cases.

DATA ANALYSIS

All data will be captured from the data collection forms and questionnaires and entered onto an electronic spreadsheet (Microsoft Excel, Microsoft Office 2015, Microsoft Corporation). Statistica will be used to analyse the data. The survey contains an array of different questions, including closed-ended, open-ended, multiple-choice and Likert-scale questions. Closed-ended questions will be scored, and one mark will be given for every correct answer according to a memo, see Appendix E. For all the scored ''knowledge'' questions a total score of 34 marks will be used. This total score will be analysed by comparing the proportion or percentage scored out of the total, of the 3 sample groups, using inter-quantile ranges or medians. The open-ended questions will either be scored according to a memo, or they will be analysed qualitatively by finding and describing common trends among the responses. For the multiple-choice questions, categorical data will be analysed using percentages and compared against the 3 sample groups. Discrete numerical data will be used for the total number of patients seen and analysed using a mean. The Likert-scale questions will be analysed by comparing the medians between the 3 sample groups.

Source of Bias

Respondent loss bias could be a source of bias where emails with links to the survey will not be taken as the participants might not participate in the study. Limitations to this online survey include a poor response as emailed questionnaires generally have a low response rate possibly due to the length of the questionnaire. Recall bias may occur as participants rely on their memory of events and may, therefore, omit details. Furthermore, incomplete entries of the survey could add to the limitations of this study, as participants may not complete or leave out certain questions.

ETHICS

The ethical principles of confidentiality will be maintained at all times during the study. Ethics clearance will be obtained from the University of the Witwatersrand's Human Research Ethics Committee.

TIMING

Gantt Chart: adapted from *Aldous et al.* 2016

Actions	Jan 2020	Feb 2020	June 2020	July 2020	Sept 2020	Oct 2020-Jan 2021	June-Oct 2021	Nov 2021	Nov-	Feb 2022
Define Research Question										
Literature Review										
Monitor Literature and add to review										
Research Week										
Refine protocol with supervisor										
Submit protocol to DRAG										
Submit protocol for ethics approval										
Await study approval										
Data collection										
Finalisation of data collection										
Data Analysis										
Refine article with supervisors										
Submit article for publication										

FUNDING

The researcher will bear any incidental expenses.

Item Description	**Cost**	
Survey Monkey	R7020	
Printing and Ink	R1000	
Prezi	R600	
Statistician: analysis of data	R5400	
Internet: data	R1245	
Total Project cost		R15 265

PROBLEMS

The Covid-19 Pandemic has cancelled many conferences and academic gatherings due to the nature of transmission of the virus. Therefore, only electronic surveys can be utilised in this instance.

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APPENDIX

A- Cross-Functional Flow Chart

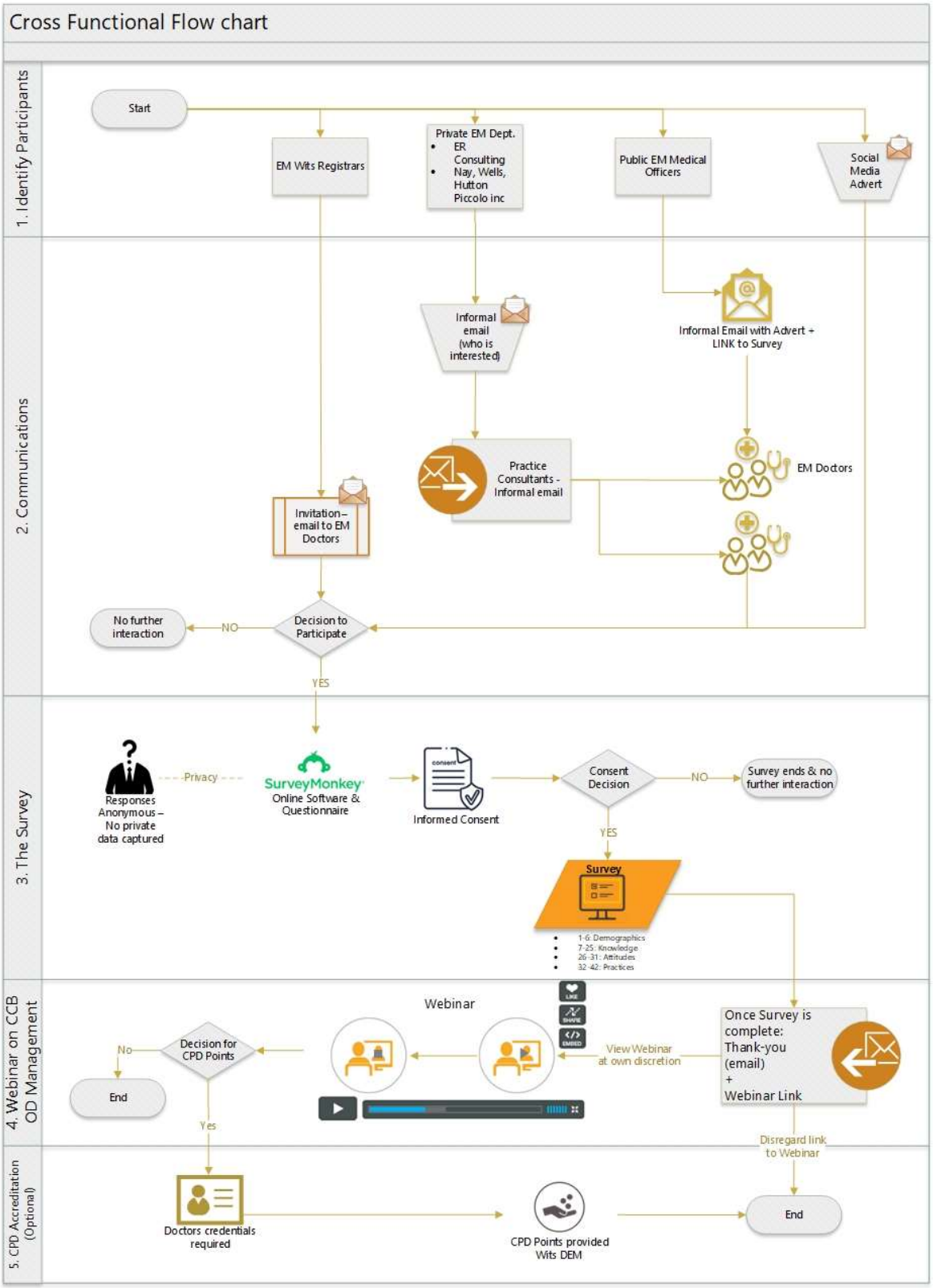
B- Information: Invitation email

C- Informal Email/ Social media Advertisement

D- Questionnaire

E- Questionnaire mark sheet for closed-ended questions

Appendix A: Cross-Functional Flow Chart



Appendix B: Invitation email

The knowledge, attitude and practice of emergency department doctors in the management of calcium channel blocker overdose in South Africa

Dear doctor,

My name is Nakita Pluymers, and I am an emergency medicine registrar. You are invited to complete the following survey for my MMED, which is focused on the knowledge, attitude and practice of emergency department doctors in the management of calcium channel blocker overdose in South Africa. One of the reasons for doing this project would be to gather information from such a survey in order to identify specific areas which are lacking, need improvement or need implementation of protocols.

Please click the link at the end of this email to start the survey. This will take approximately 20-30 minutes to complete. The survey will maintain complete anonymity. It is important to note, once you have submitted your answer(s) for each question you will not be able to review and edit your answer(s). Once the survey has been completed, an email will be sent to you with a link to a pre-recorded webinar, lasting 30 minutes, on the emergency management of calcium channel blocker overdose in the emergency department to watch at your discretion. If you wish to obtain CPD points for the webinar, please email ishmael.hlungwane@wits.ac.za with your credentials, your full name and surname and HPCSA number, for the CPD accreditation. Full anonymity will remain as WITS DEM will not have access to the survey results.

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.
If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Participation in this study is voluntary, and you can withdraw at any time. If after reading this email, you decide against participating in the study, please be assured that any further treatment will not be affected. If you have further questions, please ask me.
Thank you for reading this Study Information Sheet.

Kind Regards,

Dr Nakita Pluymers
Email: 2418919@students.wits.ac.za
Cell:0722250582

Appendix C:

See page 12 of publication submission format.

Appendix D:

See page 12 of publication submission format.

Appendix E:

See page 20 of publication submission format.

Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr N Pluymers

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M201053

NAME: (Principal Investigator)	Dr N Pluymers
DEPARTMENT:	School of Clinical Medicine Deparment of Medicine Division of Emergency Medicine Medical School University
PROJECT TITLE:	*The knowledge, attitude and practice of emergency department doctors in the management of calcium channel blocker overdose in South Africa*
DATE CONSIDERED:	2020/10/30
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr V Stephen and Professor M Wells
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2021/01/25

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **October** and therefore reports and re-certification will be due in the month of **October** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator _____ Date _____