Refractory Life-threatening Arrthythmias

HKSCCM inter hospital meeting

12/3/2013

By Dr Bobby King

PYNEH

Case 1

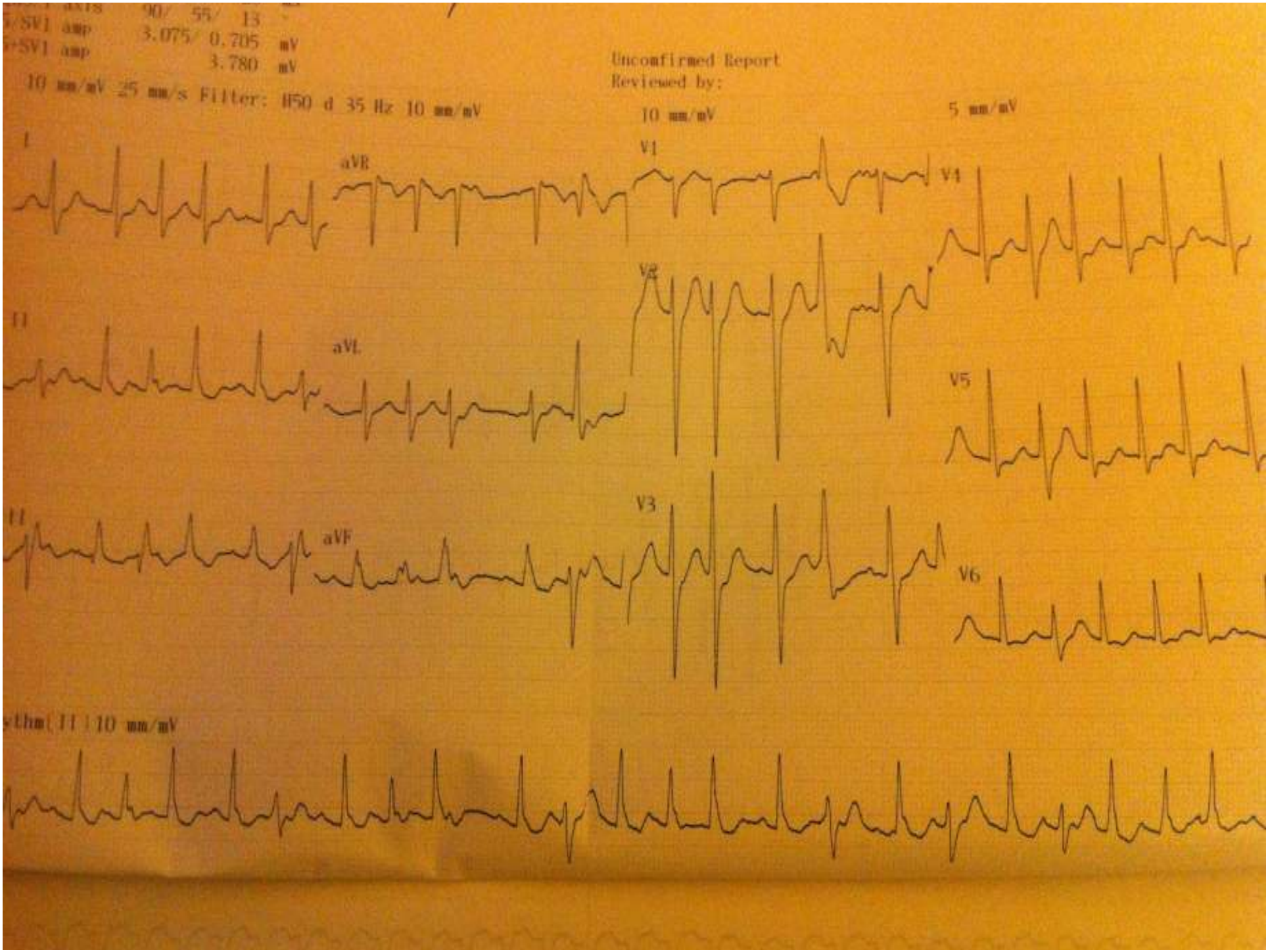
M/46

- Good past health
- Recent URTI symptoms, TOCC –ve
- Attended herbalist 1 day before and herbs was taken → no other signs and symptoms developed
- Attended the herbalist again on day of admission, herbal tea was taken at ~ 16:00
- Developed dizziness and vomiting 3 hours afterwards, face and upper limb numbness+

- Physical findings:
  - Initial GCS 15/15
  - Pupils 3+/3+
  - SaO2 90% on room air
  - BP 95/75, P 61

Progress – A&E

- Developed syncope for ~2-3 mins
- GCS E4V1M1, pupils 3-/3-
- Borderline BP 84/33, P 130
- Cardiac monitor: ventricular tachycardia
- Synchronized cardioversion 150J x 1 given
- Intubated at A&E for airway protection
- Transient hypotension responded to fluid
- Amiodarone bolus and activated charcoal was given


90/ 55/ 13
3.075/ 0.705 mV
3.780 mV
Uncomfirmed Report
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10 mm/mV 25 mm/s Filter: H50 d 35 Hz 10 mm/mV
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5 mm/mV
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
10 mm/mV

Progress in ICU

- On ventilator
- BP 129/71, P 130
- Continued on amiodarone infusion
- ventricular bigeminy+
- Herbal prescription traced, contains 制草烏
- Blood/urine sample sent to HK toxicology reference lab
- Returned to sinus rhythm on the same night

- BP remained stable, no further ventricular ectopics noted
- Extubated 4 hours after admission to ICU
- Covered with augmentin for kick of fever
- Amiodarone infusion stopped and discharged to general ward on the next day
- Discharged home after staying in EMW for 1 day

Toxicology report

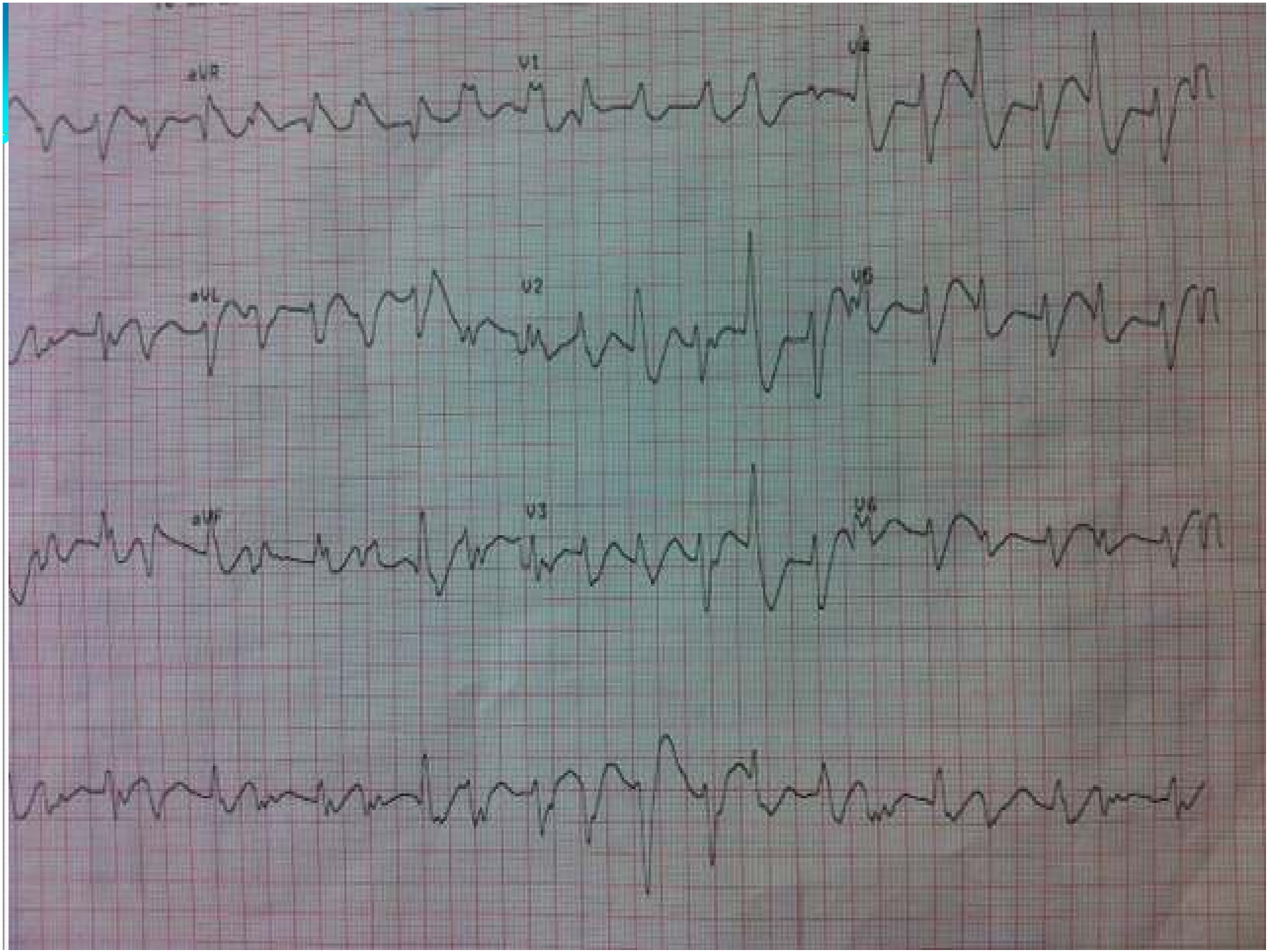
- Herbal formula:
  - 制草烏 9g (recommended dosage 1.5-3g)
  - 麻黃, associated with tachycardia or arrhythmia
  - 細辛 9g (recommended dosage 1-3g, cause arrhythmia when overdosed)
- Urine sample:
  - Aconitum alkaloids and their hydrolyzed products were detected

Case 2

M/62

- Good past health
- No recent URTI symptoms
- Habit of taking herbal tea every morning (same pack of tea > 1 month)
- Develop circumoral numbness and chest pain for 30mins after intake

- Physical findings:
  - Dual looking but GCS 15/15
  - Pupils 3+/3+
  - SaO2 93% on room air
  - BP 108/88, P 164
  - H'stix 7.0
- Cardiac monitor tracing: Ventricular tachycardia


aVR
V1
V4
aVL
V2
V5
aVF
V3
V6

Progress – A&E

- Recurrent polymorphic VT with repeated cardioversion/ defibrillation
- Witnessed cardiac arrest x 2, transient CPR required at AED
- Amiodarone was given but failed to revert back to sinus rhythm
- Intubated and CCU was consulted

Progress in CCU

- Bedside Echo: fair LV systolic function
- Proceed to urgent coronary cath. -> normal finding
- Started on IABP and VA-ECMO to support haemodynamics
  - IABP set via L femoral artery
  - VA-ECMO
    - Fr 15 A cannula to R femoral artery
    - Fr 18 V cannula from R femoral vein

Progress in ICU

- cTnI <0.03. ECG: widened QRS.
- Empirical $NaHCO_3$ given for suspected aconitine poisoning.
- Herbs sent for toxicology analysis.
- QRS became narrow and back to sinus rhythm in the same evening.
- Repeated bedside Echo: Preserved LV systolic function, no RWMA

Progress in ICU

- Haemodynamically stable all along.
- Weaned off VA-ECMO the next day by surgical decannulation and repair.
- Condition stable with no significant arrhythmia noted after VA-ECMO weaned off.
- IABP removed on the same day.
- Weaned off ventilatory support and extubated on day 2

Progress - Med

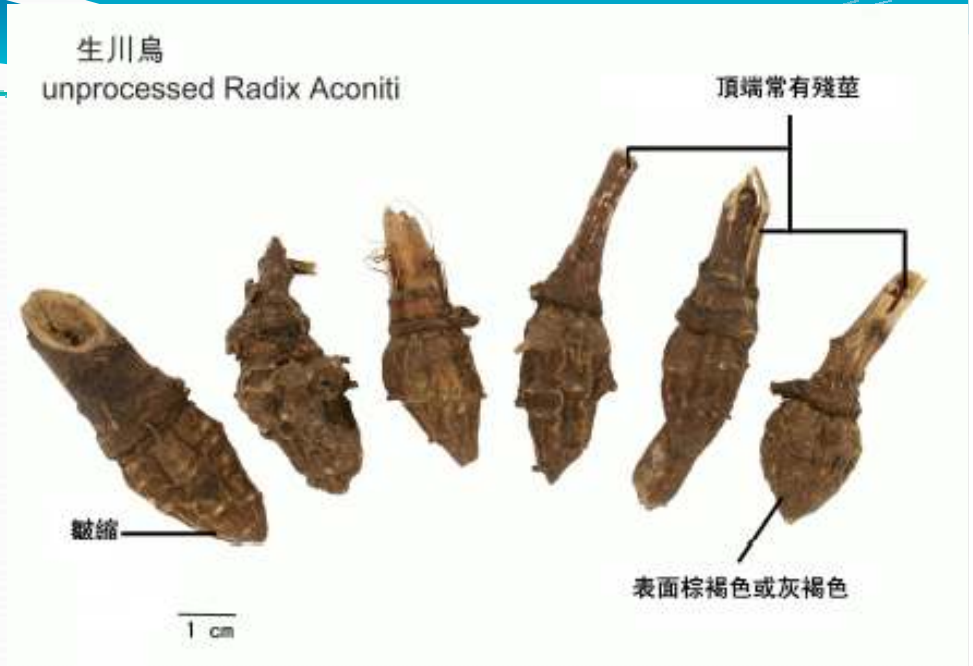
- Sputum on admission: MRSA. Treated with a course of vancomycin.
- No more VT
- Urine toxicology confirmed aconitine
- Private MRI heart normal, no evidence of arrhythmogenic right ventricular dysplasia
- Patient refused adrenaline provocation test to look for catecholaminergic polymorphic ventricular tachycardia
  (CPVT)

Toxicology report

- Herbal remnant and urine sample:
  - aconitum alkaloids (aconitine, mesaconitine, deoxyaconitine)
  - Hydrolysed products (benzoyl-aconine)
- Comment:
  - Clinical presentation, laboratory findings of aconitum alkaloids in urine and herbal remnant were compatible with aconite poisoning. ?contamination by aconitum alkaloid-containing herbs

Aconitine

- made from dried root tubers of :
- 川烏
- 草烏
- 附子



Aconitine toxicology

- Binds preferentially to the open stage of voltage-gated sodium channels, resulting in a hyperpolarized state and permanent activation.
- Main toxicity involves organ systems that rely heavily on these channels, namely cardiovascular and nervous systems.

Clinical features

- Acute onset, ranging from half an hour to several hours.
- CVS features: palpitation, hypotension, bradycardia, arrhythmia
- Neurological features: fatigue, dizziness, circumoral numbness.
- GI: nausea, vomiting, and less often abdominal pain and diarrhoea.

Treatment

- Supportive
- No specific treatment or antidote.
- Sodium bicarbonate

- ?Refractory life-threatening arrhythmias

- Aconite poisoning managed with a ventricular assist device
  - Fitzpatrick AJ et al, Anaesthesia and intensive care, 12/1994, Volume 22, Issue 6, p.714
    - Aconite poisoning managed with CPB and a ventricular assist device

- TOX-ACLS: Toxicologic-Oriented Advanced Cardiac Life Support
  - Albertson et al, Annals of emergency medicine 37:4 April 2001
    - The use of circulatory assist devices (such as the IABP or emergency cardiopulmonary bypass) may be lifesaving in patients with drug-induced shock *refractory to maximal medical therapy*.

- Two survival cases of severe aconite poisoning by percutaneous cardiopulmonary support system and cardiopulmonary bypass for fatal arrhythmia: a case report
  - *H Niinuma et al, The international Journal of Pharmacology. 2003 Volume 2 Number 1*

- Extracorporeal life support to terminate refractory ventricular tachycardia
  - Feng-Chun Tsai et al, Critical Care Medicine 2007 Vol.35, No.7
    - 11 patients suffering from ventricular tachycardia refractory to antiarrhythmia agents and cardioversion attempts were treated with ECLS
    - 9 patients were weaned and discharged with normal cardiac function
    - 1 patient had permanent brain injury and 1 succumbed to multiple organ failure

- AHA proposed that ECPR should be considered for *in-hospital* patients in cardiac arrest
  - When the duration of no-flow arrest is brief
  - The condition leading to the cardiac arrest is reversible or
  - Amenable to heart transplantation or revascularization

- Successful extracorporeal life support in cardiac arrest with recurrent ventricular fibrillation unresponsive to standard cardiopulmonary resuscitation
  - Jae-Seung Shin et al, Resuscitation (2007) 73, 309-313
    - A 37-year old out-of-hospital cardiac arrest patient who received prolonged CPR followed by ECPR.
    - The patient was discharged without neurological complications

- Extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest: A review of the Japanese literature
  - Naoto Morimura et al, Resuscitation 82 (2011) 10-14
    - An in-depth review of 139 cases
    - Out-of-hospital cardiac arrest of cardiac and non-cardiac causes
    - With ECPR

Table 3
Comparison of survival-to-hospital discharge between cases with cardiac and non-cardiac aetiology, and comparison between cases with shockable and non-shockable rhythm in the in-depth review.

	Survival	*n*	OR [lower 95%, higher 95%]	*p*
Cardiac aetiology—no. (%)	43 (59.1)	76	0.73 [0.29, 1.87]	0.51
Non-cardiac aetiology—no. (%)	16 (79.2)	25		
Total	59 (58.4)	101		
Shokable rhythm (VF, pulseless VT)	33 (70.2)	47	4.02 [1.32, 12.41]	0.01
Non-shockable rhythm (asystole, PEA)	7 (36.8)	19		
Total	40 (60.6)	66		

- No statistically significant difference between cardiac and non-cardiac aetiology
- Survival rate at discharge was statistically higher among cases with shockable rhythm

Table 4
Aetiology and neurological outcome in the in-depth review.

Etiology	*n*	(%)	Outcome at discharge (Glasgow Outcome Scale)						GR of GOS (%)		Favourable outcome of GOS (GR or MD) (%)	
			GR	MD	SD	VS	D	Not recorded*	Exclude*	Include*	Exclude*	Include*
ACS	43	30.9	18		1	2	19	3	41.9	45.0	41.9	45.0
Arrythmia	22	15.8	13	1			8		59.1	59.1	63.6	63.6
Hypothremia	19	13.7	12		1		5	1	63.2	66.7	63.2	66.7
Overdose	10	7.2	9				1		90.0	90.0	90.0	90.0
Myopathy	8	5.8	3	1			3	1	37.5	42.9	50.0	57.1
Trauma	3	2.2	1				2		33.3	33.3	33.3	33.3
Myocarditis	7	5.0	2	1		1	3		28.6	28.6	42.9	42.9
PE	4	2.9	1				2	1	25.0	33.3	25.0	33.3
Asthma	2	1.4	1				1		50.0	50.0	50.0	50.0
Renal failure	2	1.4	1				1		50.0	50.0	50.0	50.0
Drowning	2	1.4	1			1			50.0	50.0	50.0	50.0
Neck hanging	1	0.7	1						100.0	100.0	100.0	100.0
AAD	1	0.7					1		0.0	0.0	0.0	0.0
SAH	1	0.7					1		0.0	0.0	0.0	0.0
Unknown	2	1.4			1		1		0.0	0.0	0.0	0.0
No description	12	8.6	4	1			4	3	33.3	44.4	41.7	55.6
Total	139	100	67	4	3	4	52	9	48.2	51.5	51.1	54.6

* "Exclude" means "% calculated by excluding the number of not-recorded cases from a population". "Include" means "% calculated by including the total number of cases in a population".

- Key points:
  - Results suggest that ECPR may provide a higher survival rate than conventional CPR
  - Most neurological outcomes at discharge were good recovery or death

- Limitations:
  - Patient selection bias: ECPR in younger patients, witnessed arrest, by-stander CPR, etc.

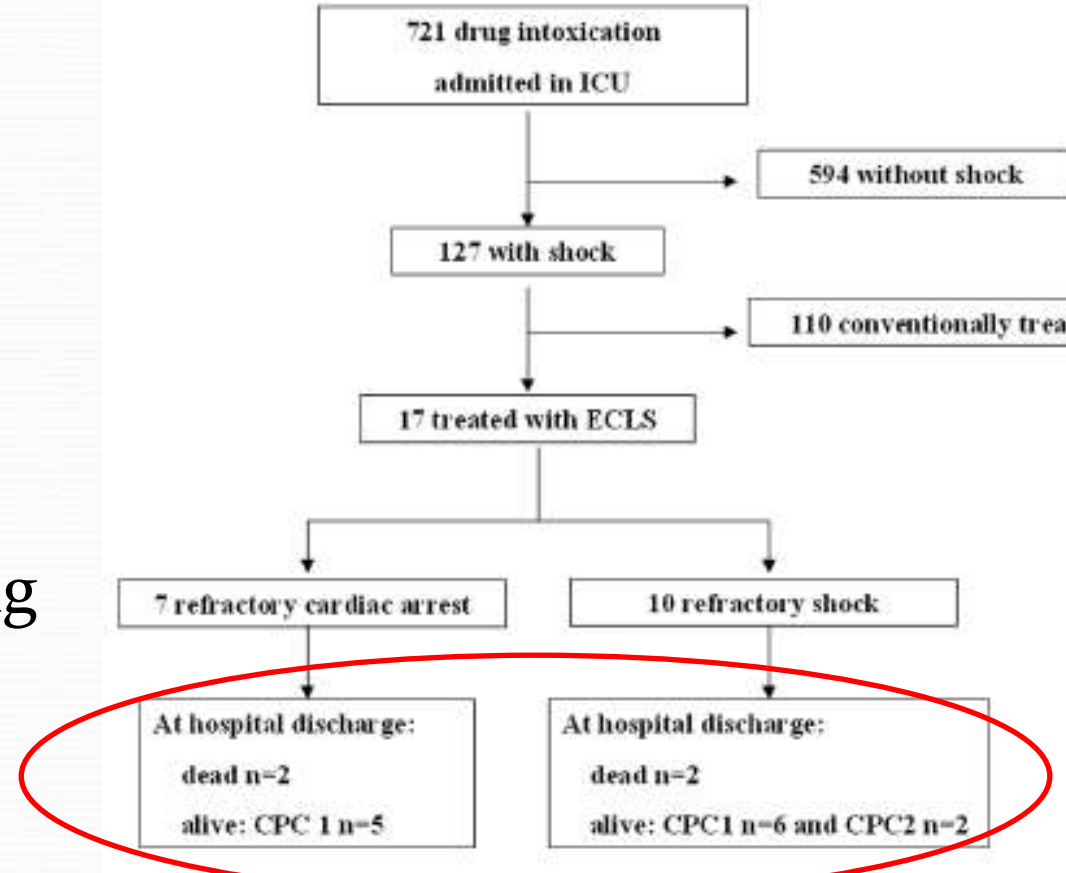
- Clinical review: Aggressive management and extracorporeal support for drug-induced cardiotoxicity
  - Frederic J Baud et al, Critical Care 2007, 11:207

- Key points:
  - Experimental evidence on animal studies showed that ECLS is life-saving in comparison with ACLS-treated animals (dogs, swine) when poisoned with membrane-stabilizing agents (lidocaine, desipramine, amitriptyline)
  - Case reports of ECLS in imipramine, desipramine, carbamazepine, propranolol, acebutolol, disopyramide, quinidine, flecainaide, verapamil, digoxin and chloroquine poisonings
  - Global survival rate of poisoned patients having benefited from ECLS is about 79%

- Extracorporeal life support in severe drug intoxication: a retrospective cohort study of seventeen cases
  - Cedric Daubin et al, Critical Care 2009, 13:R138
    - A retrospective cohort study
    - 17 patients with prolonged cardiac arrest or refractory shock following a drug overdose
    - Not responding to optimal conventional treatment

- Refractory cardiac arrest: absence of ROSC after continuous CPR >45 mins
- Refractory shock: shock not responding to optimal conventional treatment

Figure 1



Flow chart indicating patient characteristics. CPC: cerebral performance class; ECLS: extra corporeal life support; ICU: intensive care unit.

Table 1

Patients and drugs used

Patients	Drugs
1	Sotalol 4.8 g, verapamil 7.2 g
2	Disopyramide* 10 g, alprazolam 10 mg
3	Acebutolol* 10 g, méprobamate 4 g, aspirin 15 g, alprazolam 10 mg
4	Tianeptine, Bromazepam, fluoxetine, zolpidem 4 g
5	Verapamil 1.2 g, propanolol* 4 g, betaxolol 6.8 g
6	Acebutolol* 8 g, meprobamate 5 g
7	Flecaine*8 g, venlafaxine
8	Verapamil
9	Disopyramide* 3 g, lithium 7.5 g, citalopram 0.2 g
10	Propanolol* 2 g, meprobamate, paroxetine, paracetamol, dextropropoxyfene
11	Metoprolol, alcohol
12	Verapamil 3.6 g
13	Propanolol* 2 g, alcohol
14	Cibenzoline*, benzodiazepines
15	Tramadol 10 g, hydroxyzine 6 g, gabapertine 1 g, clonazepam 80 mg
16	Propafénone*, alcohol, oxilamine
17	Propanolol*

* Drugs with membrane stabilizing activity (MSA).

Table 2

Baseline characteristics at the time of ECLS implantation*

N°	ECM (min)	GCS	HR	AP (mmHg)	Vasopressor	ECG	LVEF	Lactate (mmol/L)	Bicarbonate (mmol/L)
1§	160	3	0	0	Epinephrine	Asystole	Akinesia	-	21.1
2§¶	150	3	0	0	Epinephrine	Asystole	-	> 30	17.8
3§¶	170	3	0	0	Epinephrine Isoproterenol	Asystole	Akinesia	10.8	19
4	60	3	40	60/40	Epinephrine	Bradycardia (QRS 183 ms)	Hypokinesia (LEVF 15%)	5.85	29.6
5	70	3	0	0	Epinephrine	Asystole	-	7.3	26.3
6	50	3	0	0	-	Asystole	Akinesia	-	-
7	60	3	30	50/33	Epinephrine Dobutamine	Bradycardia (QRS 214 ms)	Akinesia	-	17.5
8¶	No	3	60	50/30	Epinephrine Isoproterenol	Sinusal	-	10.5	17.7
9	No	3	40	85/54	Epinephrine Isoproterenol Dobutamine	Bradycardia (QRS 175 ms)	Hypokinesia	9.65	19.6
10¶	No	3	68	71/52	Epinephrine Dobutamine	Sinusal	Hypokinesia (LVEF 20%)	0.57	17.2
11	No	3		60/48	Epinephrine Dobutamine	Sinusal	Hypokinesia (LVEF 20%)	-	-
12	No	8	30	70/40	Norepinephrine Isoproterenol Dopamine	Atrio-ventricular block	Hypokinesia (LVEF 25%)	4.6	17.9
13**	No	3	55	75/50	Epinephrine	Sinusal	Hypokinesia (LVEF 30%)	5.9	11.7
14§¶	No	3	140	85/58	Epinephrine	Ventricular tachycardia	Hypokinesia (LVEF 20%)	8,8	20.2
15**¶	No	3	85	82/56	Epinephrine Norepinephrine	Right bundle-branch block	Hypokinesia (LVEF 25%)	1.7	18
16	No	15	60	70/60	Epinephrine	Bradycardia (QRS 203 ms)	Hypokinesia (LVEF 10%)	3.7	22.4
17	No	15	36	60/40	Epinephrine Dobutamine	Sinusal	Hypokinesia (LVEF 10%)	3.7	19.9

* For patients with cardiac arrest, we provided data recorded just before cardiac arrest if available
** ECLS performed after restoration of spontaneous circulation following a brief period of asystole
§ Patients with temporary external transthoracic electrostimulation before initiation of ECLS
¶ Patients requiring continuous venovenous hemofiltration or conventional dialysis before or immediately following ECLS implantation
AP: arterial pressure; ECG: echocardiogram; ECM: manual external cardiac massage; ECLS: extra corporeal life support; HR: heart rate; GCS: Glasgow coma score; LVEF: left ventricular ejection fraction; QRS: duration of the complex representing ventricular depolarization on electrocardiogram.

Table 3

ECLS feasibility, duration and complications

N°	Time from admission to initiation ECLS (hours)	Time to implant ECLS* (min)	Initial ECLS flow rate (l/min)	ECLS duration (days)	LVEF at ECLS discharge	Long term surviving
1**	2.5	60	3.5	2	-	No
2**	1.5	60	3	3	-	No
3	2 hours 50 mins	40	3.5	2.3	62%	Yes
4	1	60	3.5	2.5	> 50%	Yes
5	1	60	-	2.5	76%	Yes
6	1	60	3.5	2.3	-	Yes
7	6	60	3.6	3	56%	Yes
8	5	60	3.7	11	-	No
9	6	60	3.4	5	normal	No
10	24	60	4	5	42%	Yes
11	4	60	-	4	38%	Yes
12	2	60	4	6	> 50%	Yes
13	2.5	45	2.6	7	74%	Yes
14	15	90	4	6	45%	Yes
15	16	60	2.5	8	45%	Yes
16	3	60	3.5	4	50%	Yes
17	17	40	3.5	3	40%	Yes

* Delay between ECLS decision and time at which ECLS flow was provided
** Patients dead during ECLS assistance
ECLS: extra corporeal life support; LVEF: left ventricular ejection fraction.

- Clinical outcomes:
  - 15 patients were weaned off ECLS
    - 13 patients survived and were discharged without significant cardiovascular/neurological sequalae
    - 2 patients died of septic shock and cerebral death during the hospital stay
  - 2 patients withdrawn from support because of refractory multiorgan failure and cerebral death
  - High survival rate of 76% supports ECLS as an efficient rescue treatment

- ECLS complications:
  - Significant cannulation-related injuries of femoral vessels were reported in 10 patients:
    - 6 patients with limb ischaemia, 3 of them requiring urgent revascularization
    - 1 femoral thrombus
    - 1 inferior vena caval thrombus
    - 2 severe bleeding at the site of cannulation requiring a surgical revision

- ECLS related complications reported in other case reports/series:
  - Femoral nerve palsy
  - Retroperitoneal haemorrhage
  - Compartment syndrome secondary to limb ischaemia
  - Severe hypotension 4 hours after ECLS cessation
  - Pulmonary oedema requiring emergency decompression of left atrium

- Extracorporeal Cardiopulmonary Resuscitation for Patients with Out-of-Hospital Cardiac Arrest of Cardiac Origin: A Propensity-Matched Study and Predictor Analysis
  - Maekawa et al, Critical Care Medicine 2013; volume 41, number 5
    - To compare neurologic outcome following ECPR and conventional CPR and determine potential predictors that can identify candidates for ECPR
    - Intact survival rate was higher in ECPR group (29.2% -7/24 vs. 8.3% - 2/24)
    - Only pupil diameter on hospital arrival was associated with neurologic outcome (adjusted HR, 1.39 per 1-mm increase, p=0.008)

Conclusions

- ECLS maybe considered as an efficient and relatively safe therapeutic option in critically ill poisoned patients, who do not respond to conventional therapies

- Further studies are needed to clarify the criteria for unresponsiveness to conventional treatment and the indications of ECLS