

THE LAZARUS PHENOMENON

V. Adhiyaman, Specialist Registrar, Geriatric/General Medicine, Glan Clwyd Hospital, Rhyl, and
R. Sundaram, Specialist Registrar, Department of Anaesthetics, The John Radcliffe Hospital, Oxford

The boundaries that divide Life from Death are at best shadowy and vague.

Edgar Allan Poe: *Premature Burial*; 1844

INTRODUCTION

An interesting article appeared in the *Daily Post* recently outlining the case of a 70-year-old man who had suffered a cardiac arrest in a hospital. After a 15 minute period, resuscitation efforts were halted due to lack of response. Despite this, 40 minutes later circulation and spontaneous respiration were detected. However, the patient only survived for the next three days, having suffered hypoxic brain injury. On post mortem examination, the cause of death was established as myocardial infarction.¹

The family of the man and the staff involved in the incident were caused tremendous anguish and distress, which prompted the writing of this article.

Cardiac arrest followed by cardio-pulmonary resuscitation (CPR) is a very common event in hospitals and in the community. A recent community study has reported the incidence of cardiac arrest and CPR from all causes as 68 per 100,000 per year.² In this study, even though 40% survived the arrest, only 11% survived to discharge. However, the proportion of patients surviving in-hospital cardiac arrest is higher and is gradually increasing. A study involving patients who had in-hospital CPR between 1983–91 showed that about 60% survive the arrest and 32% survive to hospital discharge.³

Cardio-pulmonary resuscitation is terminated when the patient recovers, when further efforts are considered inappropriate in the best interests of the patient or when there is cardiovascular unresponsiveness in spite of adequate advanced life support (ALS). In the latter, death usually follows soon after stopping CPR. However, return of spontaneous circulation (ROSC) after cessation of CPR has been reported, albeit very rarely.

HISTORY

Return of spontaneous circulation after cessation of CPR was first described by Linko *et al.* in 1982.⁴ They reported on three patients, of which one recovered completely and was discharged home. Soon afterwards, a similar scenario was reported where the patient survived and went home.⁵ However, it took 13 years for the next case to appear in any literature when Bray used the term 'Lazarus phenomenon' (LP) to describe the delayed return

of intrinsic circulation after cessation of CPR, coining the term from the story of Lazarus,⁶ the biblical character who was resurrected by Christ four days after his death.⁷

Though LP is rare, many feel that it is grossly under-reported due to various reasons such as fear of accusation of negligence or causing of unnecessary anguish to the family. This is probably true because many clinicians – when questioned – seem to recall similar occurrences, but have not reported them in the literature. To date, only 28 cases (including the newspaper report cited above) have been published in the literature (MedLine, Pubmed).⁸⁻²¹

The name of Lazarus has been invoked to describe many other entities in which unexpected and scientifically inexplicable phenomena have happened. The 'Lazarus complex' describes the psychological sequence in the survivors of cardiac arrest and unexpected remission in Acquired Immune Deficiency Syndrome.^{22,23} Spontaneous movement in brain dead patients and in patients with spinal cord injury has been described as 'Lazarus sign'.²⁴ The term LP was also used to describe the unexpected survival of renal graft.²⁵ Survival of species after mass extinction has been called the 'Lazarus effect'.²⁷

LITERATURE

Information about the diagnoses of the cardiorespiratory arrest duration of CPR, interval between cessation of CPR and detection of LP, and the findings at autopsy, is incomplete in many of the published case reports. Of the 28 reported cases, nine had suffered a myocardial infarction and eight had obstructive airways disease (six with chronic obstructive airways disease and two with bronchial asthma). Others' diagnoses were 'pulmonary oedema', pulmonary embolism, pulmonary artery rupture, renal failure, stroke, anaemia, Addisonian crisis, pancreatitis, liver resection and trauma. At the time of cessation of CPR, 17 patients were in asystole, nine were in electro-mechanical dissociation (EMD) or pulseless electrical activity (PEA), one was in ventricular fibrillation (VF) and the rhythm was not known in one patient (see Table 1).

Return of spontaneous circulation was detected within the first five minutes in 12 patients, between five to ten minutes in two patients and after ten minutes in five patients. In nine patients, the duration between cessation of CPR and the detection of ROSC is not known. However, the exact time when ROSC occurred is difficult

TABLE 1
Summary of published case reports.

No.	Diagnosis	Age (years)	Time 1 (min)	Rhythm	Time 2 (min)	Time 3 (days)	Recovery	Ref
1	MI	68	75	ASY	20	90	Y	4
2	MI/PE	84	10	ASY	NK	6	N	4
3	MI	67	10	ASY	Some	15	N	4
4	MI/PO	80	20	ASY	5	>5	Y	5
5	Trauma	40	30	ASY	10	>90	NK	8
6	Asthma	36	25	PEA	3	>180	Y	9
7	Addison's	49	30	ASY	5	>14	Y	10
8	NK	NK	NK	ASY	NK	>1	N	10
9	Stroke	75	20	ASY	5	<1	N	10
10	NK	NK	NK	ASY	NK	<1	N	10
11	NK	NK	NK	ASY	NK	<1	N	10
12	Liver R	NK	NK	PEA	15	>1	Y	10
13	COPD	64	20	PEA	15	<1	N	11
14	Asthma	87	25	PEA	Few	12	N	12
15	PR	75	23	ASY	5	>2	N	6
16	RF	70	26	ASY	8–10	>21	Y	13
17	MI	66	30	VF	Few	NK	NK	14
18	Anaemia	71	35	ASY	Few	NK	Y	14
19	RF	55	30	ASY	7	3	N	15
20	COPE	NK	NK	PEA	NK	NK	NK	16
21	COPD	NK	NK	PEA	NK	NK	NK	16
22	COPD	NK	NK	PEA	NK	NK	NK	16
23	MI	35	88	NK	NK	<1	N	17
24	MI	54	50	PEA	Seconds	>93	Y	18
25	Stroke	80	30	ASY	5	2	N	19
26	MI	67	35	ASY	13	9	N	20
27	COPD	76	30	ASY	5	1	N	21
28	MI/COPD	70	15	PEA	45	3	N	1

Abbreviations

Time 1	duration of CPR
Time 2	time between cessation of CPR and detection of ROSC
Time 3	duration of survival after LP
Ref	reference
MI	myocardial infarction
PE	pulmonary emboli
PO	pulmonary oedema
NK	not known
Liver R	liver resection
COPD	chronic obstructive pulmonary disease
PR	pulmonary artery rupture
RF	renal failure
ASY	asystole
PEA	pulseless electrical activity
VF	ventricular fibrillation

to establish because the majority of patients were not monitored after the CPR was terminated. After ROSC, eight patients returned to their previous functional status and were discharged home. Fifteen patients did not recover their previous functional status; of these, 13 died within the next three to 15 days, and the longevity of the other two patients is not known. In five patients, the outcome is not known.

THEORIES

Many theories have been put forward to explain LP, including hyperkalemia, delayed action of drugs, transient asystole after defibrillation, oculo-cardiac reflex and pressure changes within the chest during dynamic hyperinflation. Hyperkalemia is a well known cause of EMD and could be easily ruled out, but serum potassium was found to be high in only two of the published cases.¹³ ¹⁵ Transient asystole after defibrillation is a well-recognised phenomenon and the ALS protocol advises that cardiac rhythm should be checked immediately after and one minute after defibrillation. However, in many cases of LP, patients had been in asystole or EMD for quite some time before the cessation of CPR, and so hyperkalemia and transient asystole may not explain most of the cases of LP.

Dynamic hyperinflation during positive pressure ventilation is a recognised cause of EMD during CPR in patients with obstructive airways disease.^{9, 11} In such patients, rapid ventilation may produce hyperinflation of the chest leading to elevated end-expiratory pressure (auto-PEEP). This in turn can lead to decreased venous return and cardiac output, and the circulation could be undetectable even in the presence of a perfusable cardiac rhythm. Cessation of CPR may permit return of venous flow and spontaneous circulation. Lapinsky and Leung reviewed 89 patients who had suffered in-hospital cardiac arrests:¹⁶ 34 patients had EMD, of which 13 had obstructive airways disease. Three of these 13 patients had unexpected ROSC after discontinuation of ventilation. Dynamic hyperinflation is a plausible explanation, and could explain eight out of 28 cases of LP who had obstructive airways disease. However, this may not explain the situation where ventilation was not stopped but ROSC was still detected.¹⁹

Another theory that has so far not been fully explored is 'myocardial stunning'. After brief periods of myocardial ischaemia, prolonged myocardial dysfunction can occur, followed by gradual recovery and improvement in cardiac output: this condition is termed as myocardial stunning.²⁸ Such hearts may not recover normal function for hours. Since in most myocardial infarctions a mixture of necrotic and partially ischaemic tissue occurs, myocardial stunning produced by ischaemia and followed by delayed recovery is a possible mechanism for LP in patients with myocardial infarction. Nine out of 28 patients with LP had suffered myocardial infarction, but the true incidence could not

be estimated because not all deceased patients were submitted to a post mortem examination, and it is unclear from the reports whether the diagnosis was actively sought in all cases.

MEDICO-LEGAL IMPLICATIONS OF LP

Occurrence of LP, however rare, has serious medico-legal and ethical implications, not least potential allegations of negligence and incompetence. The two most important questions might be whether ALS was conducted according to the protocol and whether it was stopped too soon. The conduct of ALS can only be assessed from the contemporaneous case record, and so it is therefore vital to record the events during cardiac arrest and attempted resuscitation as accurately as possible. At present there is no consensus concerning the timing of discontinuation of CPR. It still remains a medical decision and it is important to document the reason for termination of CPR.

PREVENTION OF LP

Is it possible to prevent LP? Frölich has suggested that CPR should be continued until ineffectiveness has been shown by decreasing blood pH despite adequate ventilation.²⁰ However, there are no defined pH values below which it has been shown to be futile to proceed with CPR, and Fumeaux *et al.* have reported a patient who made a complete recovery after cessation of CPR at a pH of 6.54.¹⁸ Lapinsky and Leung suggest that rapid ventilation should be avoided during CPR, and if EMD persists, ventilation should be discontinued for 10–30 seconds to observe for ROSC.

Others have suggested monitoring end-tidal carbon dioxide.²⁹ Several studies have stressed its prognostic value during CPR, and values greater than 10–15 mm Hg have been shown to indicate a favourable prognosis.³⁰ However, none of the case reports on LP have capnography data, and it is possible that end-tidal carbon dioxide could go below the critical value if there is transient cessation of circulation in an already compromised patient. Also, in the majority of the hospitals, measurement of end-tidal carbon dioxide is not possible outside the intensive care setting. Maleck *et al.* suggest that the patient should be further monitored for at least ten minutes after CPR has been abandoned as this is the average time interval for LP to occur.

PROCEDURES AFTER STOPPING CPR

No guidelines exist on how to monitor or treat patients after CPR has been discontinued. One has to realise that death should not be certified immediately after termination of CPR. In most cases, some form of activity is present for a few minutes after stopping CPR, like exhalation of trapped air and persistent electrical activity of the heart on a monitor. It would be wise to wait until these activities settle before certifying death. However, cardiac rhythm is not always monitored after termination

of CPR and on occasions it may take a long time before complete asystole occurs, so whether one should wait until asystole occurs before certifying death remains a controversial issue.

CERTIFICATION OF DEATH

Confirmation of death is a very important medico-legal duty of a doctor. Unlike brainstem death, there are no strict criteria in relation to death certification in general. The previously well-known definition of death as the 'irreversible cessation of spontaneous respiration and circulation' is no longer accepted widely. Death is not an event, but a process. The conference of Medical Royal Colleges in the UK advocated that death is a process during which various organs supporting the continuation of life fail,³¹ and in this context cessation of circulation and respiration should be pathognomonic. However, no elucidation of any criteria to certify death has been made.

Bernat and colleagues contemplate two sets of criteria: permanent loss of cardiopulmonary function, and the total and irreversible loss of whole brain function.³² The physical findings to support the loss of cardiopulmonary function (permanent absence of heartbeat and respiration) are the traditional and most widely used criteria to enable a doctor to certify death. The tests to confirm the irreversible cessation of whole brain functioning are not widely used and may be impossible in everyday practice. Since the absence of cardiopulmonary function alone is not a sign of definitive death, it is quite possible to declare death based on this during the interval between cessation of CPR and ROSC.

In some countries death cannot be certified unless at least one of the definitive signs of death, such as decapitation, appearance of livor mortis, rigor mortis or decomposition, or satisfactorily demonstrated brainstem death is present.¹⁹ However, these are not used universally, not always practical and may not be acceptable in many situations. Since most cases of LP occur within ten minutes, it is sensible to wait for at least ten minutes before certifying death or informing the family. In this interim period the family could be informed that CPR has been stopped because of poor response and that further efforts are not in the best interests of the patient. It should also be mentioned that the patient is being closely monitored to establish the onset of death beyond any doubt.

PROGNOSIS AFTER LP

Thirty per cent of the patients had complete recovery and were discharged home neurologically intact. The majority of the patients had suffered irreversible hypoxic brain injury. No correlation can be shown between the time interval for LP and neurological status on recovery; it was also not possible to identify any prognostic factors from the case reports.

ANY OTHER LAZARUS?

Lazarus is not unique in his survival after death. The Old Testament illustrates at least two other instances. A lifeless child was brought to Elijah the prophet: Elijah prayed to the Lord and stretched himself upon the child three times and the child survived. This is probably the first ever documented event of resuscitation.³³ Elisha was a disciple of Elijah who was summoned after a boy had collapsed and died. He arrived several hours later, prayed to the Lord, placed himself over the child and put his mouth on his mouth, eyes on his eyes and hands on his hands; the boy became warm, sneezed seven times and came back to life. In Hindu mythology, Sathyavan was caught under a falling tree and the Lord of death (Yamaraj) takes his life away. Sathyavan's wife Savithri follows the Lord and argues with him for more than an hour and wins back the life of her husband. These stories illustrate that humanity's preoccupation with death and resurrection is universal.

SUMMARY

Lazarus phenomenon is rare but probably under-reported. So far the scientific explanations for it have been inadequate. The medical profession should be aware of LP and should exercise caution while certifying death and informing the family of this immediately after termination of CPR. No current universally accepted guidelines are available on termination of CPR, monitoring after cessation of CPR and subsequent certification of death. Until such consensus is reached, it is prudent to develop local guidelines to prevent distress and anguish amongst all involved.

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