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Jeffrey R. Bender
Kerry S. Russell
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Oxford American Handbook of Cardiology

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Oxford American Handbook of Cardiology

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Preface

Despite major advances in prevention and treatment, cardiovascular disease remains the leading cause of death in the United States. There are greater than 1.4 million myocardial infarcts per year. Furthermore, the incidence of atrial fibrillation and of heart failure is rising, in part due to increased survival following acute coronary events, to our aging population, and to other undetermined factors. Management of cardiovascular disease spans a wide range, from acute care of the hemodynamically unstable patient, interventions directed at acute coronary obstructions and electrically unstable rhythms, to disease prevention and care of the chronically ill. In an era of genome-wide scans and growing lists of cardiovascular disease genes, we still require a careful and detailed understanding of disease pathophysiology and management.

In this Handbook, we attempt to represent this wide range of cardiovascular disease. We are fortunate to practice in this era of evidence-based medicine, in which care algorithms are developed and therapeutic approaches are carefully defined. The chapters of this Handbook provide the pathophysiological basis for many of these approaches, followed by delineation of management. Although these chapters will not replace the time-dependent accumulation of experience in clinical care, we hope that this Handbook provides easy and rapid access to many major day-to-day management approaches to patients with cardiovascular problems. We hope it will appeal to a broad range of clinicians in many settings, including the coronary care unit, interventional laboratories, emergency departments, and medicine units, both inpatient and outpatient. It is designed to be a rapid reference guide for practicing cardiologists, internists, and relevant trainees.

There should still be sufficient space in white coat pockets for a handbook such as this one. It is our hope that pearls of cardiovascular care will be easily removed from these white pockets and extracted from our *Handbook of Cardiology*.

Acknowledgments

We, the four editors of the *Oxford American Handbook of Cardiology*, would like to express our gratitude to all contributors. This includes the chapter authors, who are all members of the Yale University Cardiovascular Medicine Division, either junior faculty or senior fellows. They carefully have reviewed the most recent data and recommendations for cardiovascular care, incorporating the latest large clinical trials and published recommendations of our largest cardiovascular organizations, the American Heart Association and the American College of Cardiology. Thus, this represents the most up-to-date guidelines and recommendations.

We also acknowledge all involved at Oxford University Press, most notably Andrea Seils, Senior Editor of Clinical Medicine. We are particularly grateful for Andrea's patience, as the coordination of this handbook production took longer than expected.

Most importantly, we want to formally and emphatically display our gratitude to Professors Ramrakha, Hill and all the authors of the original, U.K. version of the *Oxford Handbook of Cardiology*. They all did extraordinary work, assembling the original Handbook. Much of that work has been retained in the U.S. version. As noted, we have attempted to incorporate U.S. guidelines and recently published data into the new Handbook. However, many of the original chapters remain state-of-the-art, and required very little editing or conversion. The work done by the U.K. authors was more than the foundation for the U.S. version. If approval and commendations are forthcoming, as we hope they are, these must be directed to both the U.K. and U.S. authors.

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Contents

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Detailed contents

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Symbols and Abbreviations

AAA	Abdominal aortic aneurysm
ABC	airway, breathing, circulation
ABG	arterial blood gas
ACC	American College of Cardiology
ACE	angiotensin-converting enzyme
ACLS	advanced cardiac life support
ACS	acute coronary syndrome; acute ST change
AD	after-depolarization
AED	automated external defibrillator
AF	atrial fibrillation
AFB	acid-fast bacillus
AFP	α-fetoprotein
AHA	American Heart Association
AICD	automatic implantable cardioverter defibrillator
AIH	aortic intramural hematoma
AMI	acute myocardial infarction
ANA	antinuclear antibody
ANP	atrial natriuretic peptide
AP	accessory pathway
APC	atrial premature complex
AR	aortic regurgitation
ARB	angiotensin II receptor blocker
ARDS	acute respiratory distress syndrome
ARVC	arrhythmogenic right ventricular cardiomyopathy
ARVD	arrhythmogenic right ventricular dysplasia
AS	aortic stenosis
ASA	acetylsalicylic acid
ASD	atrial septal defect
ASH	asymmetric septal hypertrophy
AST	aspartamine transferase
ATP	Adult Treatment Panel
AV	atrioventricular
AVN	atrioventricular node
AVNRT	Atrioventricular nodal reentry tachycardia
AVR	aortic valve replacement
AVRT	atrioventricular reentry tachycardia
BB	β-Blocker

bid	twice a day
BLS	basic life support
BMI	body mass index
BMS	bare metal stent
BNP	B-type natriuretic protein
BP	blood pressure
bpm	beats per minute
BUN	blood urea nitrogen
CABG	coronary artery bypass graft
CAC	coronary artery calcium
CAD	coronary artery disease
CAP	community-acquired pneumonia
CBC	complete blood count
CCB	calcium channel blocker
CCS	Canadian Cardiac Society
CCU	coronary care unit
CEA	carcinoembryonic antigen
CHB	complete heart block
CHF	congestive heart failure
CHD	congenital heart disease
CK	creatinine kinase
CMR	cardiac MRI
CMV	cytomegalovirus
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPR	cardiopulmonary resuscitation
CRP	C-reactive protein
CRT	cardiac resynchronization therapy
CS	coronary sinus
CSNRT	corrected sinus node recovery time
CT	computerized tomography
CTO	chronic total occlusion
CVD	cardiovascular disease
CVP	central venous pressure
CW	continuous wave
CXR	chest radiograph
DBP	diastolic blood pressure
DCM	diluted cardiomyopathy
DES	drug-eluting stent
DFT	defibrillation threshold testing

DI	dimensionless index
DIC	disseminated intravascular coagulation
DM	diabetes mellitus
DT	deceleration time
DVT	deep vein thrombosis
EBCT	electron beam computed tomography
EBV	Epstein–Barr virus
ECG	electrocardiogram
ECHO	echocardiogram
EDD	end diastolic dimension
EF	ejection fraction
Egram	electrogram
EMD	electromechanical dissociation
EPS	electrophysiological study
ERNA	equilibrium nuclide angiography
EROA	effective regurgitant orifice area
ERP	effective refractory period
ERT	estrogen replacement therapy
ESD	end systolic dimension
ESR	erythrocyte sedimentation rate
ET	endotracheal
ETT	exercise treadmill testing
FDA	U.S. Food and Drug Administration
FFP	fresh frozen plasma
FFR	fractional flow response
GFR	glomerular filtration rate
GI	gastrointestinal
gp	glycoprotein
Hb	hemoglobin
HDL	high-density lipoprotein
HIS	His bundle
HOCM	hypertrophic obstructive cardiomyopathy
HR	heart rate
HRA	high right atrium
HRT	hormone replacement therapy
HSVPB	His synchronous ventricular premature beat
HTN	hypertension
IABD	intra-aortic balloon pump
ICD	implantable cardiac defibrillator
ICMP	ischemic cardiomyopathy
ICU	intensive care unit

IE	infective endocarditis
IGF	insulin-like growth factor
IHD	ischemic heart disease
IJV	internal jugular vein
IM	intramuscular
INR	International Normalized Ratio
IO	intraosseous
ISFC	International Society and Federation Cardiology
ISR	in-stent restenosis
IV	intravenous
IVC	inferior vena cava
IVP	intravenous push
IVRT	isovolumic relaxation time
IVUS	intravascular ultrasound
JVP	jugular venous pressure
LA	left atrium, atrial
LAD	left anterior descending (artery)
LAO	left anterior oblique
LBBB	left bundle branch block
LDH	lactate dehydrogenase
LDL	low-density lipotprotein
LFTs	liver function tests
LMS	left main stent
LMWH	low-molecular-weight heparin
LQTS	long QT syndrome
LV	left ventricular
LVAD	left ventricular assist device
LVEDP	left ventricular end diastolic pressure
LVF	left ventricular failure
LVH	left ventricular hypertrophy
LVOT	left ventricular outflow tract
MACE	major adverse cardiac event(s)
MDCT	multidetector computed tomography
MI	myocardial infarction
MPI	myocardial perfusion imaging
MR	mitral regurgitation; magnetic resonance
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MVP	mitral valve prolapse
MVR	mitral valve replacement
NCEP	National Cholesterol Education Program

NCT	narrow complex tachycardia
NG	nasogastric
NO	nitric oxide
NPPE	negative pressure pulmonary edema
NPPV	noninvasive positive pressure ventilation
nREM	non-rapid eye movement sleep
NSAID	nonsteroidal anti-inflammatory drug
NSTEMI	non-ST elevation myocardial infarction
NYHA	New York Heart Association
OCP	oral contraceptive pill
OCT	optical coherence tomography
OM	obtuse marginal brach
OTC	over-the-counter (drugs)
OTW	over the wire
PA	pulmonary artery
PAD	peripheral arterial disease
PAN	polyarteritis nodosa
PCI	percutaneous coronary intervention
PCWP	pulmonary capillary wedge pressure
PDA	posterior descending artery
PDEI	phosphodiesterase inhibitor
PDGF	platelet-derived growth factor
PE	pulmonary embolus
PEA	pulseless electrical activity
PEEP	positive end expiratory pressure
PEFR	peak expiratory flow rate
PEG	percutaneous endoscopic gastrostomy
PET	positron emission tomography
PFO	patent foramen ovale
PHS	Physicians Health Study
PISA	proximal isovelocity surface area
PLAX	parasternal long axis
PMBV	percutaneous balloon mitral valuloplasty
PMT	pacemaker-mediated tachycardia
po	orally/by mouth
PR	pulmonary regurgitation
prn	as required
PS	pulmonary stenosis
PSAX	parasternal short axis
PTCA	percutaneous transluminal coronary intervention
PTFE	polytetrafluoroethylene

PV	pulmonary valve
PVE	prosthetic valve endocarditis
PVR	pulmonary vascular resistance
qid	four times a day
RA	rheumatoid arthritis; right atrium, atrial
RAS	renal artery stenosis
RBBB	right bundle branch block
RBC	red blood cells
RCA	right coronary artery
RF	radiofrequency; rheumatoid factor
RFA	radio frequency ablation
RHC	right heart catheterization
RIJ	right interior jugular
rtPA	recombinant tissue-type plasminogen activator
RV	right ventricular; regurgitant volume
RVA	right ventricular apex
RVAD	right ventricular assist device
RVF	right ventricular failure
RVH	right ventricular hypertrophy
RVOT	right ventricular outflow tract
RVSP	right ventricular systolic pressure
SACT	sinoatrial conduction time
SAH	subarachnoid hemorrhage
SAM	systolic anterior motion
SAN	sinoatrial node
SBE	subacute bacterial endocarditis
SBP	systolic blood pressure
SC	subcutaneous; subcostal
SCD	sudden cardiac death
SCM	sternocleidomastoid
SCV	subclavian vein
SK	streptokinase
SL	sublingual
SLE	systemic lupus erythematosus
SND	sinal node dysfunction
SNRT	sinus node reentrant tachycardia
SPECT	single photon electron computed tomography
SR	sinus rhythm
SS	suprasternal
STEMI	ST elevation myocardial infarction
SV	stroke volume

SVC	superior vena cava
SVG	saphenous vein graft
SVT	supraventricular tachycardia
TAA	thoracic aortic aneurysm
TB	tuberculosis
TCL	tachycardia cycle length
TDI	tissue Doppler imaging
TdP	torsades de pointes
TEE	transesophageal echocardiography
TFT	thyroid function test
TGF-β	transforming growth factor β
TIA	transient ischemic attack
tid	three times a day
TOF	tetralogy of Fallot
TR	tricuspid regurgitation
TS	tricuspid stenosis
TSH	thyroid-stimulating hormone
TST	tuberculin skin test
TTE	transthoracic echocardiogram
TV	tricuspid valve
TVI	time–velocity index
UA	unstable angina
UFH	unfractionated heparin
VF	ventricular fibrillation
VLDL	very low density lipoprotein
VMA	vanilmandelic acid
VPB	ventricular premature beats
VPC	ventricular premature complex
V/Q	ventilation–perfusion ratio
VSD	ventricular septal defect
VT	ventricular tachycardia
VVI	ventricular demand pacing
WBC	white blood cells
WCL	Wenckebach cycle length
WCT	wide complex tachycardia
WHO	World Health Organization
WMSI	wall motion score index
WPW	Wolff–Parkinson–White (syndrome)

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Chapter 1

Cardiovascular emergencies and practical procedures

Cardiovascular emergencies

Adult basic life support

Basic life support (BLS) is the backbone of effective resuscitation following a cardiorespiratory arrest. The aim is to maintain adequate ventilation and circulation until the underlying cause for the arrest can be reversed. A period of 3–4 minutes without adequate perfusion (less if the patient is hypoxic) will lead to irreversible cerebral damage.

Occasionally you will be the first to discover the unresponsive patient, and it is important to rapidly assess the patient and begin cardiopulmonary resuscitation (CPR). The various stages in BLS are described here and summarized in Figure 1.1.

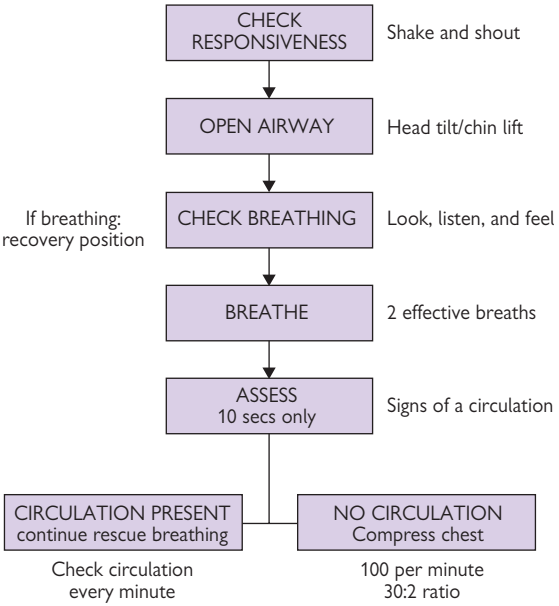


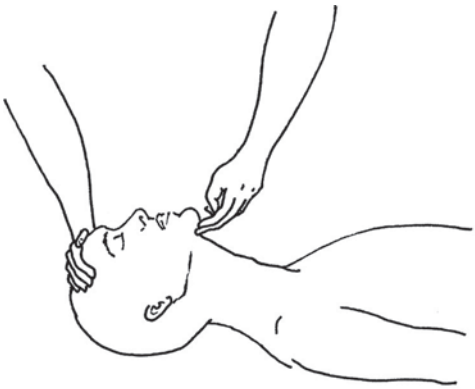
Figure 1.1 Stages in basic life support. For further information, see BLS/ACLS AHA/ACC guidelines.

1. Assessment of the patient

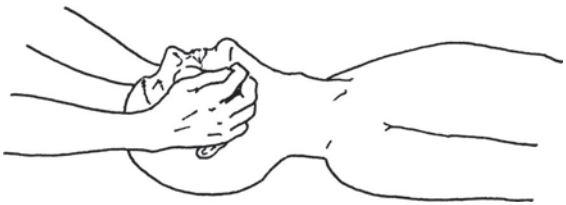
- **Ensure safety of rescuer and victim.**
- **Check whether the patient is responsive**. Gently shake the victim and ask loudly, "Are you all right?"
  - If the victim responds, place them in recovery position and get help.
  - If the victim is unresponsive, shout for help and move on to assess airway (see below).

2. Airway assessment

- **Open the airway**. With two fingertips under the point of the chin, tilt the head up. If this fails, place your fingers behind the angles of the lower jaw and apply steady pressure upward and forward. Remove ill-fitting dentures and any obvious obstruction. If the patient starts breathing, roll patient over into the recovery position and try to keep the airway open until an orophyrangeal airway can be inserted. Use jaw thrust without head extension, if trauma is suspected (see Fig. 1.2).



Jaw lift to open the airway



Jaw thrust (thrust the angle of the mandible upward)

Figure 1.2 Opening the airway. Reproduced with permission from Ramrakha PS, Moore KPK (2004). *Oxford Handbook of Acute Medicine*. Oxford, UK: Oxford University Press.

- **Keep the airway open; look, listen, and feel for breathing**. Look for chest movements, listen at the victim's mouth for breathing sounds, and feel for air on your cheek (for no more than 10 seconds).
  - If the patient is breathing, turn patient into the recovery position, check for continued breathing, and get help.
  - If the patient is not breathing or is making occasional gasps or weak attempts at breathing, send someone (or go for help if alone). (On return) Start rescue breaths by giving two slow effective breaths, each resulting in a visible rise and fall in the chest wall; a mouth-to-barrier device may be used.

3. Assessment of circulation

- Assess signs of circulation by feeling the carotid pulse for no more than 10 seconds.
  - If there are signs of circulation but no breathing, continue rescue breaths and check for signs of breathing every 10 breaths.
  - If there are no signs of circulation, start chest compression. Combine rescue breaths and compression at the rate of 30 compressions to two effective breaths, repeating this cycle 5 times in approximately 2 minutes.
- The ratio of compressions to lung inflation remains the same for resuscitation with two persons.

Adult advanced life support

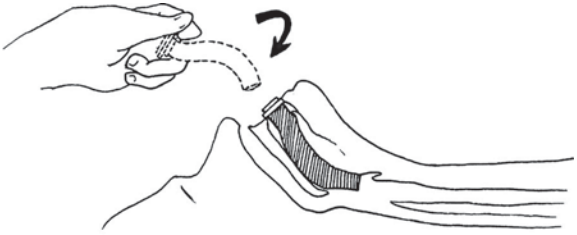
It is unlikely that an effective spontaneous cardiac activity will be restored by BLS without more advanced techniques (intubation for effective ventilation, drugs, defibrillation, etc.). Do not waste time. As soon as help arrives, delegate CPR to someone less experienced in advanced cardiac life support (ACLS), so that you are able to continue.

- Attach the patient to an automated external defibrillator (AED) as soon as possible to determine if there is a shockable rhythm and treat appropriately (see p. 7 for the universal treatment algorithm).
- Oropharyngeal or nasopharyngeal airways help maintain the patency of the airway by keeping the tongue out of the way (see Fig. 1.3). Endotracheal (ET) intubation is the best method of securing the airway. *Do not attempt this if you are inexperienced.*
- Establish venous access. Central vein cannulation (internal jugular or subclavian) is ideal but requires more training and practice and is not for the inexperienced. If venous access fails, drugs may be given via an intraosseous (IO) route (more effective than an ET tube) or ET tube into the lungs (except for bicarbonate and calcium salts). Double the dose of drug if using this route, as absorption is less efficient than when given intravenously (IV).

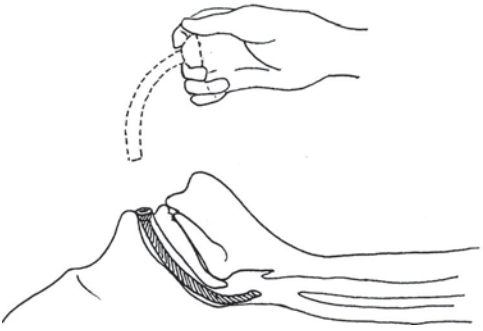
Post resuscitation care

- ***Try to establish the events*** that precipitated the arrest from the history, staff, witnesses, and hospital notes of the patient. Is there an obvious cause (myocardial infarction [MI], hypoxia, hypoglycemia, stroke, drug overdose or interaction, electrolyte abnormality, etc.)? Record the duration of the arrest in the notes with the interventions, drugs (and doses) in chronological order.
- ***Examine the patient*** to check that both lung fields are being ventilated; check for ribs that may have broken during CPR. Listen for any cardiac murmurs. Check the neck veins. Examine the abdomen for an aneurysm or signs of peritoneal irritation. Insert urinary catheter. Consider a nasogastric (NG) tube if the patient remains unconscious. Record the Glasgow Coma Score and perform a brief neurological assessment.
- ***Investigations:*** **ECG** (electrocardiogram; looking for MI, ischemia, tall T-waves [suggesting hyperkalemia]); **ABG** (arterial blood gas; mixed metabolic and respiratory acidosis is common and usually responds to adequate oxygenation and ventilation once the circulation is restored); **CXR** (chest X-ray; check position of ET tube, look for pneumothorax); and glucose, **CBC** (complete blood count).
- After early and successful resuscitation from a primary cardiac arrest, the patient may rapidly recover completely. The patient must be transferred to an appropriate location (ICU) for monitoring and treatment.
- Change any venous lines that were inserted at the time of arrest for central lines inserted with sterile technique. Insert an arterial line and consider pulmonary artery (PA) catheter (Swan–Ganz) if requiring inotropes.

- Remember to talk to the relatives. Keep them informed of events and give a realistic picture of the arrest and possible outcomes.
- When appropriate, consider the possibility of organ donation and do not be frightened to discuss this with the relatives. Even if discussion with the relatives is delayed, remember that corneas and heart valves may be used up to 24 hours after death.
- Consider hypothermia for patients who do not immediately wake up, or who were "down" for a period of time.



Insertion of oropharyngeal airway



Insertion of nasopharyngeal airway

Figure 1.3 Insertion of nasopharyngeal airway. Reproduced with permission from Ramrakha PS, Moore KPK (2004). *Oxford Handbook of Acute Medicine*. Oxford, UK: Oxford University Press.

Universal treatment algorithm

Cardiac rhythms of cardiac arrest can be divided into two groups:

1. **Ventricular fibrillation/pulseless ventricular tachycardia (VF/VT).**
2. **Other cardiac rhythms,** which include **asystole** and **pulseless electrical activity (PEA)**.

The principle difference in treatment of the two groups of arrhythmias is the need for attempted defibrillation in the VF/VT group of patients.

Figure 1.4 summarizes the algorithm for management of both groups of patients.

VF/VT

VF/VT are the most common rhythms at the time of cardiac arrest. Success in treatment of VF/VT is dependent on the delivery of prompt defibrillation. With each minute the chances of successful defibrillation declines by 7%–10%.

- Chest compressions and ventilation should be undertaken until the monitor and defibrillator are available. Typically, 120J to 200J for a biphasic defibrillator and 360J for a monophasic defibrillator is delivered in one shock. Continue CPR x 5 cycles then reassess. If there is persistent VF/VT a second shock is delivered, biphasic at an energy specific to the device and monophasic at 360J. At this time, epinephrine 1 mg IV/IO or vasopressin 40 U IV/IO can be given and repeated. Next, another shock is delivered and if there is persistent VF/VT, then antiarrhythmics (amiodarone 300 mg IV/IO once, then 150 mg IV/IO once, or lidocaine 1.0–1.5 mg/kg first dose and then 0.5–0.75 mg/kg IV/IO for a maximum of 3 mg/kg) should be considered
- After each shock CPR is resumed immediately for 5 cycles, after which the carotid pulse should be palpated only if the waveform changes to one usually capable of providing a cardiac output.
- Shock cycle is repeated every minute if VF/VT persists.
- Myocardial and cerebral viability must be maintained after each shock cycle with chest compressions and ventilation.
- In between cycles of defibrillation, reversible factors must be identified and corrected, the patient intubated (if possible), and venous access obtained.

Non-VF/VT rhythms

The outcome from these rhythms is generally worse than that with VF/VT unless a reversible cause can be identified and treated promptly.

- Chest compressions and ventilation should be undertaken for 3 minutes with each loop of the algorithm (1 minute if directly after a shock).
- With each cycle, attempts must be made to intubate the patient, gain IV access, and give adrenaline.

Asystole

- Atropine 3 mg IV should be given to block all vagal output.
- In the presence of p waves on the ECG strip/monitor, pacing (external or transvenous) must be considered.

Pulseless electrical activity (PEA)

- Identification of the underlying cause and its correction are both vital for successful resuscitation. Resuscitation must be continued while reversible causes are being sought.

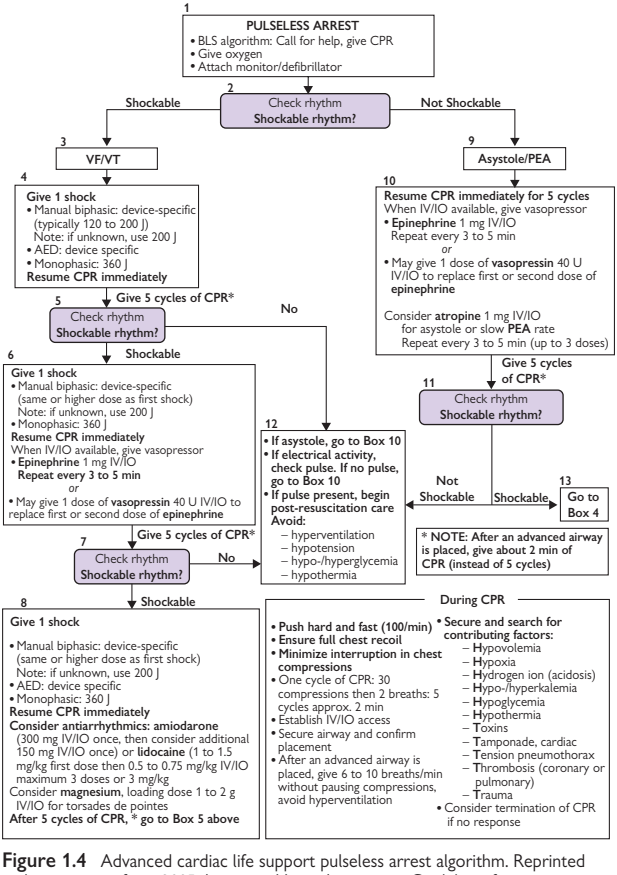


Figure 1.4 Advanced cardiac life support pulseless arrest algorithm. Reprinted with permission from 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Part 7.2: Management of Cardiac Arrest. *Circulation* 2005; 112(Suppl IV):IV58–IV66. ©2005, American Heart Association, Inc.

Acute pulmonary edema: assessment

Presentation

- Acute breathlessness, cough, frothy blood-stained (pink) sputum
- Collapse, cardiac arrest, or shock
- Associated features may reflect underlying cause:
  - Chest pain or palpitations—? ischemic cardiomyopathy (ICMP)/MI, arrhythmia
  - Preceding history of dyspnea on exertion—? ICMP, poor left ventricular (LV) function
  - Oliguria, hematuria—? acute renal failure
  - Seizures, signs of intracranial bleed

Causes

A diagnosis of pulmonary edema or "heart failure" is not adequate. Underlying causes must be sought in order to direct treatment appropriately. These may be divided into the following:

- Increased pulmonary capillary pressure (hydrostatic)
- Increased pulmonary capillary permeability
- Decreased intravascular oncotic pressure

Often a combination of factors is involved (e.g., pneumonia, hypoxia, cardiac ischemia). See Table 1.1.

The main differential diagnosis is acute exacerbation of chronic obstructive pulmonary disease (COPD) (previous history, quiet breath sounds ± wheeze, fewer crackles). It may be difficult to differentiate the two clinically.

Principles of management

1 Stabilize the patient—relieve distress and begin definitive treatment.
2 Look for an underlying cause.
3 Address hemodynamic and respiratory issues.
4 Optimize and introduce long-term therapy.

Initial rapid assessment

- If the patient is unstable (e.g., unable to speak, hypoxic, systolic blood pressure [SBP] <100 mmHg), introduce stabilizing measures and begin treatment immediately before detailed examination and investigations (see p. 12).
- If the patient is stable and/or if there is doubt as to the diagnosis, give oxygen and diuretic, but await the outcome of clinical examination, CXR, and blood tests such as B-type natriuretic peptide (BNP) level before deciding on definitive treatment.

Urgent investigations for all patients

- **ECG** — Sinus tachycardia most common.
  ? Any cardiac arrhythmia (SVT, VT).
  ? Evidence of acute ST change (ACS).
  ? Evidence of underlying heart disease (LVH, P mitrale).
- **CXR** — To confirm diagnosis, looking for interstitial shadowing, enlarged hila, prominent upper lobe vessels, pleural effusion, and Kerley B lines. Cardiomegaly may or may not be present. Also exclude pneumothorax, pulmonary embolus (oligemic lung fields), and consolidation.
- **Laboratory** — ? Pre-existing renal impairment. Regular K^+ and Mg measurements (once on IV diuretics). Anemia. Signs of infection.
- **ECHO** — As soon as practical to assess LV function, valve abnormalities, ventricular septal defect (VSD), or pericardial effusion.
- **ABG** — Typically low PaO_2, PCO_2 levels may be low (hyperventilation) or increased depending on severity. Pulse oximetry may be inadequate if peripheral vasoconstriction is present.

Pulmonary edema: causes

Table 1.1 Look for an underlying cause for pulmonary edema

Increased pulmonary capillary pressure (hydrostatic)	
↑ Left atrial (LA) pressure	• Mitral valve disease • Arrhythmia (e.g., AF) with pre-existing mitral valve disease • Left atrial myxoma
↑ Left ventricular end diastolic pressure (LVEDP)	• Ischemia • Arrhythmia • Aortic valve disease • Cardiomyopathy • Uncontrolled hypertension • Pericardial constriction • Fluid overload • High-output states (anemia, thyrotoxicosis, Paget's, atrioventricular (AV) fistula, beri-beri) • Renovascular disease
↑ Pulmonary venous pressure	• L → R shunt (e.g., VSD) • Veno-occlusive disease
Neurogenic	• Intracranial hemorrhage • Cerebral edema • Postictal
High-altitude pulmonary edema	
Increased pulmonary capillary permeability	
Acute lung injury	Acute respiratory distress syndrome (ARDS)
Decreased intravascular oncotic pressure	
Hypoalbuminemia	• ↑ Losses (e.g., nephrotic syndrome, liver failure) • ↓ Production (e.g., sepsis) • Dilution (e.g., crystalloid transfusion).

Note: the critical LA pressure for hydrostatic edema = serum albumin (g/L) x 0.57.

Pulmonary edema: management

Stabilize the patient

Patients with acute pulmonary edema should initially be continuously monitored and managed where full resuscitation facilities are available.

- Sit the patient up in bed.
- Give 100% oxygen by facemask, unless contraindicated, i.e., COPD.
- If the patient is severely distressed, the patient may require continuous positive airway pressure (CPAP) or mechanical ventilation.
- Treat any hemodynamically unstable arrhythmia (urgent synchronized DC shock may be required, (p. 78).
- Give
  - Morphine 2.5–5 mg IV (caution: abnormal ABGs)
  - Frusemide 40–120 mg slow IV injection
- Secure venous access and send blood for urgent blood work.
- Unless thrombolysis is indicated, take ABG.
- If SBP ≥90 mmHg and the patient does not have aortic stenosis:
  - Give sublingual nitroglycerin spray (2 puffs).
  - Start IV nitroglycerin infusion 1–10 mg/hr; increase the infusion rate every 15–20 minutes, titrating against blood pressure (aiming to keep SBP ~100 mmHg).
- If SBP <90 mmHg, treat patient as cardiogenic shock.
- Insert a urinary catheter to monitor urine output.
- Repeat ABG and K^+ if the clinical condition deteriorates or fails to improve, or after 2 hours if there is improvement and the original sample was abnormal.
- Monitor pulse, BP, respiratory rate, O_2 saturation with a pulse oximeter (if an accurate reading can be obtained), and urine output.

Further management

The subsequent management of the patient is aimed at ensuring adequate ventilation/gas exchange, ensuring hemodynamic stability, and correcting any reversible precipitants of acute pulmonary edema. If the patient stabilizes, begin investigations looking for a cause.

If the patient remains unstable and/or deteriorates conduct the assessments listed next.

Assess patient's respiratory function

Wheeze may be caused by interstitial pulmonary edema. If there is a history of asthma, give nebulized salbutamol (2.5–5 mg), nebulized ipratropium bromide (500 μg), and hydrocortisone (200 mg) IV.

Indications for further respiratory support

- Patient exhaustion or continuing severe breathlessness
- Persistent hypoxemia
- Rising P_aCO_2
- Persistent or worsening acidosis (pH < 7.2)

Continuous positive airway pressure (CPAP)

This may be tried for cooperative patients who can protect their airway, have adequate respiratory muscle strength, and who are not hypotensive. The positive pressure reduces venous return to the heart and may compromise BP.

Endotracheal intubation and mechanical ventilation

This may be required, and some positive end expiratory pressure (PEEP) should be used. PEEP may also lower SBP.

Discuss the patient with the on-call anesthesiologist and ICU team early.

Assess patient's hemodynamic status

It is important to distinguish between cardiogenic and noncardiogenic pulmonary edema, as further treatment is different for the two groups. Making this distinction may be difficult clinically. A central venous or PA (Swan–Ganz) catheter must be inserted if the patient's condition will allow this procedure.

Management

The general approach involves a combination of diuretics, vasodilators, ± inotropes. Patients may be divided into two groups:

- Patients in shock (with SBP <90 mmHg)
- Hemodynamically stable patients with SBP >90 mmHg

Patients with SBP <90 mmHg

The choice of inotropic agent depends on the clinical condition of the patient and, to some extent, the underlying diagnosis:

SBP <90 mmHg give:

- **Dopamine** at doses of >2.5 μg/kg/min has a pressor action in addition to direct and indirect inotropic effects and may be used at higher doses (10–20 μg/kg/min) if the blood pressure remains low. However, it tends to raise the pulmonary capillary filling pressure further and should be combined with vasodilators (e.g., nitroprusside or hydralazine) once the blood pressure is restored (see below). Beware of arrhythmias at these dosages.
- **Epinephrine** infusion may be preferred to high-dose dopamine as an alternative inotrope. Once the blood pressure is restored (>100 mmHg), vasodilators such as nitroprusside/hydralazine or nitroglycerin infusion should be added to counteract the pressor effects. Epinephrine can be combined with dobutamine and/or a phosphodiesterase inhibitor, especially in the context of a poor ventricle.
- **Dobutamine infusion** at 5 μg/kg/min, increasing by 2.5 μg/kg/min every 10–15 minutes to a maximum of 20 μg/kg/min until BP >100 mmHg. This may be combined with dopamine (2.5–5 μg/kg/min). However, tachycardia and/or hypotension secondary to peripheral vasodilation may limit its effectiveness.
- **Phosphodiesterase inhibitors** (milrinone) should be considered where dobutamine fails.

- **Intra-aortic balloon counterpulsation** should also be used with or without inotropes in the context of a potentially reversible cause for the pulmonary edema and shock (e.g., ongoing myocardial ischemia, VSD, acute mitral regurgitation [MR]).
- Further doses of diuretic may be given.

Patients with SBP ≥90 mmHg

- Further doses of diuretic may be given (furosemide 40–80 mg IV q3–4h or as a continuous infusion [10–80 mg/hr]).
- Continue the nitroglycerin infusion, increasing the infusion rate every 15–20 minutes up to 10 mg/hr, titrating against blood pressure (aiming to keep SBP ~100 mmHg).

Long-term management

- Unless a contraindication exists, start an angiotensin-converting enzyme (ACE) inhibitor, increasing the dose to as near the recommended maximum dose as possible. In the context of LV impairment, ACE inhibitors have significant prognostic benefit.
- If ACE inhibitors are contraindicated or not tolerated, consider use of hydralazine and long-acting oral nitrate in combination.
- If the patient is already on high doses of diuretics and ACE inhibitors, consider addition of spironolactone (25–50 mg) (monitor renal function and serum potassium).
- In the context of stable patients (no clinical features of failure) and poor LV function, β-blockers have significant mortality and some symptomatic benefit (start with very small dose and increase gradually every 2 weeks with regular monitoring). Bisoprolol, carvedilol, and metoprolol can all be used.
- Ensure that all arrhythmias are treated.
- Digoxin can be used for symptomatic improvement.
- Consider cardiac resynchronization therapy (biventricular pacing) in the context of severe LV dysfunction, broad QRS complex ± MR on ECHO.
- Patients in atrial fibrillation (AF) or with poor LV function should be considered for long-term anticoagulation.
- Patients <60 years with severe irreversible LV dysfunction and debilitating symptoms must be considered for cardiac transplantation.

Pulmonary edema: specific conditions

Diastolic LV dysfunction

This typically occurs in elderly hypertensive patients with left ventricular hypertrophy (LVH), where there is impaired relaxation of the ventricle in diastole. There is marked hypertension, pulmonary edema, and normal, or only mild, systolic LV impairment.

With tachycardia, diastolic filling time shortens. As the ventricle is "stiff" in diastole, LA pressure is increased and pulmonary edema occurs (exacerbated by AF as filling by atrial systole is lost).

Treatment involves control of hypertension with IV nitrates (and/or nitroprusside), calcium blockers (verapamil or nifedipine), and even certain β-blockers (e.g., carvedilol, bisoprolol) and, if appropriate, restoration of sinus rhythm.

Fluid overload

Standard measures are usually effective.

- Check that the patient is not anemic (Hb ≥10 g/dL). Remove 500 mL blood via cannula in a large vein and repeat if necessary.
- If anemic (e.g., renal failure) and acutely unwell, consider dialysis.

Known (or unknown) renal failure

- Unless the patient is permanently anuric, large doses of IV furosemide may be required in addition to standard treatment.
- If this fails or the patient is known to be anuric, dialysis will be required.
- In patients not known to have renal failure an underlying cause should be sought.

Anemia

- Cardiac failure may be worsened or precipitated by the presence of significant anemia. Symptoms may be improved in the long term by correcting this anemia.
- If the anemia is thought to be exacerbating pulmonary edema, ensure that an adequate diuresis is obtained prior to transfusion. Give slow transfusion (3–4 hours per unit) of packed cells, with IV furosemide 20–40 mg before each transfusion.

Hypoproteinemia

- Treatment involves diuretics, cautious albumin replacement, spironolactone (if there is secondary hyperaldosteronism), and treatment of the underlying cause for hypoproteinemia.

Acute aortic regurgitation

Presentation

- Sudden, severe aortic regurgitation (AR) presents as cardiogenic shock and acute pulmonary edema.
- The hemodynamic changes are markedly different from those seen in chronic AR. The previous normal-sized LV results in a smaller effective forward flow and higher LVEDP for the same degree of AR.
- Patients are often extremely unstable, tachycardic, and peripherally vasoconstricted and often have pulmonary edema. Unlike chronic AR, pulse pressure may be near normal.
- If available, ask about history of previous valvular heart disease, hypertension, features of Marfan's syndrome (family history), and risk factors for infective endocarditis.
- Physical signs of severe AR include a quiet aortic closure sound (S2); an ejection systolic murmur over the aortic valve (turbulent flow); high-pitched and short, early diastolic murmur (AR); quiet S1 (premature closure of the mitral valve).
- Examine specifically for signs of an underlying cause.
- Where there is no obvious underlying cause (e.g., acute MI), assume infective endocarditis until proven otherwise.

Causes

- Infective endocarditis
- Ascending aortic dissection
- Collagen vascular disorders (e.g., Marfan's)
- Connective tissue diseases (large- and medium-vessel arteritis)
- Trauma
- Dehiscence of a prosthetic valve

Diagnosis

Diagnosis is based on a combination of clinical features and transthoracic and/or transesophageal ECHO.

Management

Acute AR is a surgical emergency and all other management measures are only aimed at stabilizing the patient until urgent aortic valve replacement (AVR) can take place. The patient's clinical condition will determine the urgency of surgery (and risk of mortality).

General measures

- Admit the patient to intensive care unit (ICU).
- Give oxygen and begin treating any pulmonary edema with diuretics.
- Monitor blood gases; mechanical ventilation may be necessary.
- Blood cultures × 3 are essential.
- Serial ECG: watch for developing atrioventricular (AV) block or conduction defects in endocarditis.

Specific measures

- Every patient must be discussed with a cardiothoracic surgeon.
- In the context of good systemic BP, vasodilators such as sodium nitroprusside or hydralazine may temporarily improve forward flow and relieve pulmonary edema.
- Inotropic support may be necessary if the patient is hypotensive. However, inotropes are best avoided as any increase in systemic pressures and peripheral vasoconstriction may worsen AR.
- All patients with hemodynamic compromise should have immediate or urgent AVR.
- *Infective endocarditis*: indications for surgery are given on p. 208.
- Intra-aortic balloon pump (IABP) must be avoided, as it will worsen AR.

Acute mitral regurgitation

Presentation

- Patients most commonly present with acute shortness of breath and severe pulmonary edema. Symptoms may be less severe, or spontaneously improve as left atrial compliance increases. There may be a history of previous murmur, angina, or myocardial infarction.
- The signs are different from those seen in chronic MR because of the presence of a nondilated and relatively noncompliant LA. Acute MR results in a large LA systolic pressure wave (v wave) and hence pulmonary edema.
- Patients may be acutely ill with tachycardia, hypotension, peripheral vasoconstriction, and pulmonary edema, and a pan-systolic murmur of MR.
- Later in the illness, probably because of sustained high left atrial and pulmonary venous pressures, right heart failure develops.
- Examine for signs of any underlying conditions.
- When there is no obvious underlying cause (e.g., acute MI; see Box 1.1), assume the patient has infective endocarditis until proven otherwise.

Diagnosis

Diagnosis is based on a combination of clinical features and ECHO. Transthoracic echocardiography (TTE) can be used to readily diagnose and quantify MR. It also provides information on LV status (in particular regional wall motion abnormalities that can give rise to MR).

TEE can provide specific information about etiology of valve dysfunction, including papillary muscle rupture and MV leaflet (anterior and posterior) structural abnormalities. This information will be vital for a decision regarding definitive management. The important differential diagnosis is a VSD.

TTE and Doppler studies can readily differentiate between the two conditions. Alternatively, if ECHO is not available, pulmonary artery catheterization in acute MR will exclude the presence of a left-to-right shunt and the pulmonary capillary wedge pressure (PCWP) trace will demonstrate a large v-wave.

General measures

- Admit patient to ICU.
- Give oxygen and begin treating any pulmonary edema with diuretics.
- Monitor blood gases; mechanical ventilation may be necessary.
- Blood cultures × 3 are essential.
- If present, MI should be treated in the standard manner.

Specific measures

Pulmonary edema may be very resistant to treatment.

- In the presence of good BP, reduction in preload (nitroglycerin infusion) and afterload, especially with ACE inhibitors, is important. Systemic vasodilators such as hydralazine (12.5–100 mg tid) can also be added.

- An IABP will help decrease LVEDP and increase coronary blood flow.
- *Patients may require inotropic support.* There are multiple combinations and etiologies of MR and hemodynamic status, and local policy and expertise should dictate choice of agent.
- CPAP and intubation and positive-pressure ventilation are extremely useful and must be considered in all severe and/or resistant cases.
- Hemodynamic disturbance and severe pulmonary edema in the context of acute MR is a surgical emergency.
- *Infective endocarditis:* indications for surgery are given on p. 208.
- *Post-infarct MR:* management depends on the patient's condition following resuscitation. Patients who are stabilized may have mitral valve replacement (MVR) deferred because of risks of surgery in the post-infarct patient. Preoperative management should consist of diuretics and vasodilators, including ACE inhibitors, if tolerated. Opening the infarct-related artery (angioplasty) may improve acute MR.

Box 1.1 Causes of acute mitral regurgitation

- Infective endocarditis
- Papillary muscle dysfunction or rupture (post-MI).
- Rupture of chordae tendinae (e.g., infection, myxomatous degeneration, systemic lupus erythematosus [SLE])
- Trauma (to leaflets, papillary muscle, or chordae)
- Prosthetic valve malfunction (e.g., secondary to infection)
- Left atrial myxoma
- Acute rheumatic fever
- Collagen vascular disorders (e.g., Marfan's)
- Connective tissue diseases (large- and medium-vessel arteritis)

Deep vein thrombosis: assessment

Presentation

- Deep vein thrombosis (DVT) is most commonly asymptomatic. Minor leg discomfort or isolated swelling (>65%) in the affected limb are the most common clinical features. Breathlessness or chest pain may be secondary to pulmonary embolism (PE).
- Signs include erythema and swelling of the leg, dilated superficial veins, and calf discomfort on dorsiflexion of the foot (Homan's sign). The thrombus may be palpable as a fibrous cord in the popliteal fossa. Confirm the presence of swelling (>2 cm) by measuring the limb circumference 15 cm above and 10 cm below the tibial tuberosity.
- In all cases of leg swelling, abdominal and rectal (and pelvic in women) examination must be carried out to exclude an abdominal cause.

See Table 1.2 for risk factors for DVT.

Investigations

- *Real-time B-mode venous compression ultrasonography* of leg veins is largely replacing venography as the initial investigation of choice. It is quick and noninvasive, with sensitivity and specificity of over 90%, and does not carry the risk of contrast allergy or phlebitis. It can simultaneously assess extent of proximal progression of the thrombus, in particular, extension into pelvic vessels.
- *D-dimers* have a high negative predictive value for DVT. A low clinical probability of DVT and a negative D-dimer does not require further investigation. A positive D-dimer result should be followed by ultrasonography.
- *Venography:* use if results are uncertain and clinical suspicion is high.
- Consider baseline-investigation blood work.
- If appropriate, look for an underlying cause.
- *Procoagulant screen*: refer to local screening policy and get hematology advice (e.g., prothrombin time [INR] and partial thromboplastin time, C-reactive protein [CRP], erythrocyte sedimentation rate (ESR), proteins C and S, antithrombin III levels, factor V_{Leiden} mutation, auto-Ab screen, immunoglobulins and immunoelectrophoretic strip, anticardiolipin antibody, Ham test, etc.)
- *Screen for malignancy*: ultrasound ± computed tomography (CT) (abdomen and pelvis), CXR, liver function tests (LFTs), prostate-specific antigen (PSA), carcinoembryonic antigen (CEA), CA-125, CA-19.9, β-HCG, etc.

Table 1.2 Risk factors for DVT

Procoagulant states	
Congenital	*Acquired*
Factor V_{Leiden}	Malignant disease (~5%)
Antithrombin III deficiency	Antiphospholipid syndrome
Protein C deficiency	Myeloproliferative disorders
Protein S deficiency	Oral contraceptive pill (especially with Factor V_{Leiden} mutation)
	Nephrotic syndrome (via renal AT III losses)
	Homocystinuria
	Paroxysmal nocturnal hemoglobinuria
Venous stasis	
Immobility (e.g., long journeys)	Recent surgery
Pelvic mass	Pregnancy or recent childbirth
	Severe obesity
Miscellaneous	
Hyperviscosity syndromes	
Previous DVT or PE	
Family history of DVT/PE	

Deep vein thrombosis: management

If there is high clinical suspicion of DVT (the presence of risk factors and absence of an alternative diagnosis), start empiric anticoagulation with low-molecular-weight heparin (LMWH). This may be stopped if subsequent investigations are negative.

Below-knee DVT

Thrombi limited to the calf have a lower risk of embolization and may be treated with compression stockings and subcutaneous (SC) prophylactic doses of LMWH until the patient is mobile, to deter proximal propagation of thrombus. A brief period of systemic anticoagulation with LMWH may lessen the pain from below-knee DVT.

Above-knee DVT

Thrombi within the thigh veins warrant full anticoagulation with LMWH/unfractionated heparin (UFH) and subsequently with warfarin.

Anticoagulation

Heparin

- LMWHs have now superceded UFH for management of both DVT and PE. They require no monitoring on a daily basis and allow outpatient treatment.
- There must be a period of overlap between LMWH/UFH therapy and anticoagulation with warfarin until the INR is within therapeutic range and stable.
- LMWH are administered primarily as a once-daily subcutaneous (SC) injection, and dosage is determined by patient weight. It may require adjustment for renal dysfunction.

Warfarin

- Always anticoagulate with LMWH/UFH before starting warfarin. Protein C (a vitamin K–dependent anticoagulant) has a shorter half-life than that of the other coagulation factors and levels fall sooner, resulting in a transient procoagulant tendency.
- If DVT is confirmed, begin warfarin and maintain on LMWH/UFH until INR >2.
- Anticoagulate (INR 2–2.5) for 3 months.
- If there is recurrent DVT or the patient is at high risk of recurrence, consider lifelong anticoagulation.

Thrombolysis

This should be considered for recurrent, extensive, proximal venous thrombosis (e.g., femoral or iliac veins), as it is more effective than anticoagulation alone in promoting clot dissolution and produces a better clinical outcome.

Catheter-directed thrombolytic therapy (rt-PA or SK) is superior to systemic thrombolysis.

One approach is streptokinase (SK) 250,000 U over 30 minutes then 100,000 U every hour for 24–72 hours. See p. 100 for contraindications to thrombolysis.

Further management

Women taking the combined oral contraceptive pill (OCP) should be advised to stop this.

If there are contraindications to anticoagulation, consider the insertion of a caval filter to prevent PE.

All patients should be treated with thigh-high compression stockings to try to reduce symptomatic venous distension when mobilizing.

Pulmonary embolism (PE): assessment

Symptoms

- Classically presents with sudden-onset, pleuritic chest pain, associated with breathlessness and hemoptysis. Additional symptoms include postural dizziness or syncope.
- Massive PE may present as cardiac arrest (particularly with electromechanical dissociation) or shock.
- Presentation may be atypical, i.e., unexplained breathlessness or unexplained hypotension or syncope only.
- Pulmonary emboli should be suspected in all breathless patients with risk factors for DVT or with clinically proven DVT.
- Recurrent PEs may present with chronic pulmonary hypertension and progressive right heart failure.

Signs

- Examination may reveal tachycardia and tachypnea only. Look for postural hypotension (in the presence of raised jugular venous pressure [JVP]).
- Look for signs of raised right heart pressures and cor pulmonale (raised JVP with prominent a-wave, tricuspid regurgitation, parasternal heave, right ventricular S3, loud pulmonary closure sound with wide splitting of S2, pulmonary regurgitation).
- Cyanosis suggests a large PE.
- Examine for a pleural rub (may be transient) or effusion.
- Examine lower limbs for obvious thrombophlebitis.
- Mild fever (>37.5°C) may be present. There may be signs of coexisting COPD.

Causes

Most frequently PE is secondary to DVT (leg >> arm).

Other causes

- Rarely secondary to right ventricular thrombus (post-MI)
- Septic emboli (e.g., tricuspid endocarditis)
- Fat embolism (post-fracture)
- Air embolism (venous lines, diving)
- Amniotic fluid
- Parasites
- Neoplastic cells
- Foreign materials (e.g., venous catheters)

Prognostic features

The prognosis in patients with pulmonary emboli varies greatly and is associated in part with any underlying condition. Generally worse prognosis is associated with larger PE; poor prognostic indicators include the following:

- Hypotension
- Hypoxia
- ECG changes (other than nonspecific T-wave changes)

Pulmonary embolism: investigations

General investigations

- ABG — Normal ABG does not exclude a PE. ↓P_aO_2 is invariable with larger PEs. Other changes include mild respiratory alkalosis and ↓P_aCO_2 (due to tachypnea) and metabolic acidosis (secondary to shock).
- ECG — Commonly shows sinus tachycardia ± nonspecific ST- and T-wave changes in the anterior chest leads. The classical changes of acute cor pulmonale such as $S_1Q_3T_3$, right axis deviation, or right bundle branch block (RBBB) are only seen with massive PE. Less common findings include AF.
- CXR — May be normal; a near-normal chest film in the context of severe respiratory compromise is highly suggestive of a PE. Less commonly may show focal pulmonary oligemia (*Westermark's sign*), a raised hemidiaphragm, small pleural effusion, wedge-shaped pleural shadow, subsegmental atelectasis, or dilated proximal pulmonary arteries.
- Blood tests — There is no specific test. Mildly elevated CK, troponin, BNP may be seen.
- ECHO — Insensitive for diagnosis but can exclude other causes of hypotension and raised right-sided pressures (e.g., tamponade, RV infarction). In PE may show RV dilatation and global hypokinesia (with sparing of apex [*McConnell's sign*]) and pulmonary artery dilation, and Doppler may show tricuspid/pulmonary regurgitation, allowing estimation of RV systolic pressure. Rarely, the thrombus in the pulmonary artery may be visible.

Specific investigations

D-dimer

- A highly sensitive but nonspecific test.
- Useful in ruling out PE in patients with low probability.
- Results can be affected by advancing age, pregnancy, trauma, surgery, malignancy, and inflammatory states.

Ventilation/perfusion (V/Q) lung scanning

A perfusion lung scan (with IV technetium-99-labeled albumin) can be considered in suspected cases of PE, especially if there is a contraindication to giving contrast. A ventilation scan (inhaled xenon-133) in conjunction increases the specificity by assessing whether the defects in the ventilation and perfusion scans "match" or "mismatch." Pre-existing lung disease makes interpretation difficult.

A normal perfusion scan rules out significant-sized PE.

Abnormal scans are reported as low, medium, or high probability:

- A high-probability scan is strongly associated with a PE, but there is a significant minority of false positives.
- A low-probability scan with a low clinical suspicion of PE should prompt a search for another cause for the patient's symptoms.

Box 1.2 Investigations for an underlying cause for PE

- Ultrasound of deep veins of legs
- Ultrasound of abdomen and pelvis (? occult malignancy, pelvic mass, lymphadenopathy)
- CT of abdomen/pelvis
- Screen for inherited procoagulant tendency (e.g., proteins C, S, anti thrombin III, factor V_{Leiden}, etc.)
- Autoimmune screen (anticardiolipin antibody, antinuclear antibody [ANA])
- Biopsy of suspicious lymph nodes or masses

If clinical suspicion of PE is high and the scan is of low or medium probability, alternative investigations are required.

CT pulmonary angiography (CTPA)

This is the recommended initial lung imaging modality in patients with PE as long as there are no contraindications.

- It allows direct visualization of emboli as well as other potential parenchymal disease, which may provide alternative explanation for symptoms.
- Sensitivity and specificity are high (>90%) for lobar pulmonary arteries but not so high for segmental and subsegmental pulmonary arteries.
- A patient with a positive CTPA does not require further investigation.
- A patient with a negative CTPA in the context of a high or intermediate probability of a PE should undergo further investigation.

Evaluation of leg veins with ultrasound

This is not very reliable. Almost half of patients with PE do not have evidence of a DVT and thus a negative result cannot rule out a PE.

Ultrasound is a useful second-line investigation as an adjunct to a CTPA/VQ scan.

Outcome studies have demonstrated that it would be safe not to anticoagulate patients with a negative CTPA and lower limb ultrasound who have an intermediate or low probability of a PE.

Pulmonary angiography

This is the gold-standard investigation. It is indicated in patients in whom diagnosis of embolism cannot be established by noninvasive means. Look for sharp cutoff of vessels or obvious filling defects. It is an invasive investigation and can be associated with 0.5% mortality.

If there is an obvious filling defect, the catheter or a guide wire passed through the catheter may be used to disrupt the thrombus.

After angiography, the catheter may be used to give thrombolytics directly into the affected pulmonary artery (see below).

The contrast can cause systemic vasodilatation and hemodynamic collapse in hypotensive patients.

MR pulmonary angiography

Results are comparable to those of pulmonary angiography in preliminary studies. It can simultaneously assess ventricular function.

Pulmonary embolism: management

1. Stabilize the patient

- Unless an alternative diagnosis is made, the patient should be treated as for a pulmonary embolus until this can be excluded.
- Monitor cardiac rhythm, pulse, BP, and respiration rate every 15 minutes with continuous pulse oximetry and cardiac monitor. Ensure full resuscitation facilities are available.
- Obtain venous access and start IV fluids (crystalloid or colloid).
- Give maximal inspired oxygen via facemask to correct hypoxia. Mechanical ventilation may be necessary if the patient is tiring (beware of cardiovascular collapse when sedation is given for ET intubation).
- **Give LMWH or UFH to all patients with high or intermediate risk of PE until diagnosis is confirmed.** Meta-analysis of multiple trials has shown LMWH to be superior to UFH with a reduction in mortality and bleeding complications. For doses, consult local formulary.
- If there is evidence of hemodynamic instability (systemic hypotension, features of right heart failure) or cardiac arrest, patients will benefit from thrombolysis with recombinant tissue plasminogen activator (rtPA) or streptokinase (see Table 1.3; same doses used for treatment of STEMI [see p. 100]). Local delivery of thrombolytics to the site of thrombus via a PA catheter may also be considered.

2. Analgesia

- Patients may respond to oral nonsteroidal anti-inflammatory drugs.
- Opiate analgesia should be used with caution. The vasodilatation caused by these drugs may precipitate or worsen hypotension. Give small doses (1–2 mg morphine IV) slowly. Hypotension should respond to IV colloid.
- Avoid IM injections (anticoagulation and possible thrombolysis).

3. Anticoagulation

Patients with a positive diagnosis must undergo anticoagulation with warfarin. There should be a period of overlap with LMWH/UFH until INR values are therapeutic. Target INR is 2–3 for most cases.

Standard duration of anticoagulation is as follows:

- 3 months for temporary risk factor
- 3 months for first idiopathic cases
- At least 6 months for other cases
- With recurrent events and underlying predisposition to thromboembolic events (e.g., antiphospholipid antibody syndrome) lifelong anticoagulation may be needed (as well as higher target INR >3).

Table 1.3 Dosage of thrombolytic agents for pulmonary embolus

rtPA	100 mg over 2 hours or 0.6 mg/kg over 15 minutes (maximum of 50 mg) followed by heparin
Streptokinase	250,000 U over 30 minutes followed by 100,000 U/hr infusion for 24 hours

Contraindications for thrombolysis are identical to those for STEMI (p. 100).

Cardiac arrest (also see p. 5)

Massive PE may present as cardiac arrest with electromechanical dissociation (EMD). Exclude the other causes of EMD.

Hypotension

The acute increase in pulmonary vascular resistance results in right ventricular dilatation and pressure overload, which mechanically impairs LV filling and function. Patients require a higher than normal right-sided filling pressure but may be worsened by fluid overload.

- Insert an internal jugular sheath prior to anticoagulation. This can be used for access later if necessary.
- Give thrombolysis if there are no contraindications.
- If hypotensive give IV fluids.
- If hypotension persists, invasive monitoring and/or inotropic support is required. The JVP is a poor indicator of the left-sided filling pressures in such cases. Adrenaline is the inotrope of choice.
- Femorofemoral cardiopulmonary bypass may be used to support the circulation until thrombolysis or surgical embolectomy can be performed.
- Pulmonary angiography in a hypotensive patient is hazardous as the contrast may cause systemic vasodilatation and cardiovascular collapse.

Pulmonary embolectomy

In patients who have contraindications to thrombolysis and are in shock requiring inotropic support, there may be a role for embolectomy if appropriate skills are on site.

This can be performed percutaneously in the catheterization laboratory using a number of devices or surgically on cardiopulmonary bypass Percutaneous procedures may be combined with peripheral or central thrombolysis.

Seek specialist advice early. Best results are obtained before onset of cardiogenic shock.

Radiological confirmation of the extent and site of embolism is preferable before thoracotomy.

Mortality is ~25%–30%.

Inferior vena cava (IVC) filter

There is little evidence that use of an IVC filter improves short- or long-term mortality rates.

Filters are positioned percutaneously and, if possible, patients must remain anticoagulated to prevent further thrombus formation. Most IVC filters are positioned infrarenally (bird's nest filter) but can also be suprarenal (Greenfield filter).

Indications for IVC filter use include the following:

- Anticoagulation contraindicated—e.g., active bleeding, heparin-induced thrombocytopenia, planned intensive chemotherapy.
- Anticoagulation failure despite adequate therapy.
- Prophylaxis in high-risk patients—e.g., progressive venous thrombosis, severe pulmonary hypertension, extensive trauma.

Fat embolism

This is commonly seen in patients with major trauma. There is embolization of fat and microaggregates of platelets, red blood cells (RBCs), and fibrin in systemic and pulmonary circulation. Pulmonary damage may result directly from the emboli (infarction) or from chemical pneumonitis and ARDS.

Clinical features

There may be a history of fractures followed (24–48 hours later) by breathlessness, cough, hemoptysis, confusion, and rash.

Examination reveals fever (38–39°C), widespread petechial rash (25%–50%), cyanosis, and tachypnea. There may be scattered rales in the chest, although examination may be normal. Changes in mental state may be the first sign with confusion, drowsiness, seizures, and coma. Examine the eyes for conjunctival and retinal hemorrhages; occasionally fat globules may be seen in the retinal vessels.

Severe fat embolism may present as shock.

Investigations

• ABG	Hypoxia and a respiratory alkalosis (with low P_aCO_2) as for thromboembolic PE
• CBC	Thrombocytopenia, acute intravascular hemolysis
• Coagulation	Disseminated intravascular coagulation
• Chemistries and glucose	Renal failure, hypoglycemia
• Ca^{2+}	May be low
• Urine	Microscopy for fat and dipstick for hemoglobin.
• ECG	Usually nonspecific (sinus tachycardia; occasionally signs of right heart strain)
• CXR	Usually lags behind the clinical course. There may be patchy, bilateral, air space opacification. Effusions are rare
• CT head	Consider if there is a possibility of head injury with expanding subdural or epidural bleed

Differential diagnosis

This includes pulmonary thromboembolism, other causes of ARDS, septic shock, hypovolemia, cardiac or pulmonary contusion, head injury, aspiration pneumonia, and transfusion reaction.

Management

- Treat respiratory failure. Give oxygen (maximal via face mask; CPAP and mechanical ventilation if necessary).
- Ensure adequate circulating volume and cardiac output. Central venous pressure (CVP) is not a good guide to left-sided filling pressures, and a PA catheter (Swan–Ganz) may be used to guide fluid replacement. Try to keep PCWP 15–18 mmHg and give diuretics if necessary. Use inotropes to support circulation as required.

- Aspirin, heparin, and Dextran 40 (500 mL over 4–6 hours) are of some benefit in the acute stages but may exacerbate bleeding from sites of trauma.
- High-dose steroids (methylprednisolone 30 mg/kg q8h for 3 doses) have been shown to improve hypoxemia,[1] but steroids are probably most effective if given prophylactically.

1 Lindeque BG, Schoeman HS, Dommisse GF, Boeyens MC, Vlok AL (1987). Fat embolism and the fat embolism syndrome. A double-blind therapeutic study. *J Bone Joint Surg*, 69:128–131.

Hypertensive emergencies

Hypertensive crisis

Hypertensive crisis is defined as a severe elevation in BP (SBP >200 mmHg, DBP >120 mmHg). Rate of change in BP is important. A rapid rise is poorly tolerated and leads to end-organ damage, whereas a gradual rise in a patient with existent poor BP control is better tolerated. Hypertensive crises are classified as follows:

1. **Hypertensive emergency**, where a high BP is complicated by acute target organ dysfunction (see Box 1.3) and includes
- *Hypertensive emergency with retinopathy*—there is marked elevation in BP (classically DBP >140 mmHg) with retinal hemorrhages and exudates (previously called accelerated hypertension), and
- *Hypertensive emergency with papilledema* with a similarly high BP and papilledema (previously called malignant hypertension).

2. **Hypertensive urgency**, where there is a similar rise in BP but without target organ damage.

Conditions presenting as hypertensive emergency

- Essential hypertension.
- Renovascular hypertension: atheroma, fibromuscular dysplasia, acute renal artery occlusion.
- Renal parenchymal disease: acute glomerulonephritis, vasculitis, scleroderma.
- Endocrine disorders: pheochromocytoma, Cushing's syndrome, primary hyperaldosteronism, thyrotoxicosis, heperparathyroidism, acromegaly, adrenal carcinoma.
- Eclampsia and pre-eclampsia.
- Vasculitis.
- Drugs: presence of cocaine, amphetamines, MAOI interactions, or cyclosporine, or withdrawal of β-blocker or clonidine.
- Autonomic hyperactivity in the presence of spinal cord injury.
- Coarctation of the aorta.

Presentation

Occasionally there are minimal nonspecific symptoms such as mild headache and nosebleed.

A small group of patients present with symptoms resulting from BP-induced microvascular damage:

- Neurological symptoms: severe headache, nausea, vomiting, visual loss, focal neurological deficits, seizures, confusion, intracerebral hemorrhage, coma (see below)
- Chest pain (hypertensive heart disease, MI, or aortic dissection) and congestive cardiac failure
- Symptoms of renal failure: renal impairment may be chronic (secondary to long-standing hypertension) or acute (from the necrotizing vasculitis of malignant hypertension)

Patients may present with hypertension as one manifestation of an underlying "disease" (renovascular hypertension, chronic renal failure, CREST syndrome, pheochromocytoma, pregnancy).

Examination should be directed at looking for evidence of end-organ damage even if the patient is asymptomatic (heart or renal failure, retinopathy, papilledema, focal neurological symptoms).

Box 1.3 Hypertensive emergencies

- Hypertensive emergency with retinopathy/papilledema
- Hypertensive encephalopathy
- Hypertension-induced intracranial hemorrhage/stroke
- Hypertension with cardiovascular complications:
  - Aortic dissection
  - MI
  - Pulmonary edema
- Pheochromocytoma
- Pregnancy-associated hypertensive complications
  - Eclampsia and pre-eclampsia
- Acute renal insufficiency
- Hypertensive emergency secondary to acute withdrawal syndromes (e.g., β-blockers, centrally acting antihypertensives)

Hypertensive emergencies: management

Priorities in management are as follows:
1. Confirm the diagnosis and assess the severity.
2. Identify those patients needing specific emergency treatment.
3. Plan long-term treatment.

Diagnosis and severity

- Ask about previous BP recordings, previous and current treatment, sympathomimetics, antidepressants, nonprescription drugs, and recreational drugs.
- Check the blood pressure yourself, in both arms, after a period of rest and, if possible, on standing.
- Examine carefully for clinical evidence of cardiac enlargement or heart failure, peripheral pulses, renal masses, or focal neurological deficit. Always examine the fundi—dilate if necessary.

All patients should have the following tests:

• **CBC**	Microangiopathic hemolytic anemia with malignant hypertension
• **Chemistries**	Renal impairment and/or $\downarrow K^+$ (diffuse intrarenal ischemia and secondary hyperaldosteronism)
• **Coagulation screen**	Disseminated intravascular coagulation (DIC) with malignant hypertension
• **CXR**	Cardiac enlargement Aortic contour (dissection?) Pulmonary edema
• **Urinalysis**	Protein and red cells ± casts

Other investigations depending on clinical picture and possible etiology include the following:

• **24-hour urine collection**	Creatinine clearance Free catecholamines, metanephrines or vanilmandellic acid (VMA)
• **ECHO**	LVH, aortic dissection
• **Renal US and Doppler**	Size of kidneys and renal artery stenosis
• **MR renal angiogram**	Renal artery stenosis
• **CT/MR brain**	Intracranial bleed
• **Drug screen**	Cocaine, amphetamine, others

Indications for admission

- Diastolic blood pressure persistently ≥120 mmHg
- Retinal hemorrhages, exudates or papilledema
- Renal impairment

Treatment principles

- **Rapid reduction in BP is unnecessary, must be avoided, and can be very dangerous**. This can result in cerebral and cardiac hypoperfusion (abrupt change of >25% in BP will exceed cerebral BP autoregulation).
- Initial BP reduction (of 25%) should be achieved over 1–4 hours with a less rapid reduction over 24 hours to a diastolic blood pressure (DBP) of 100 mmHg.
- The only two situations where BP must be lowered rapidly are in the context of aortic dissection and MI.

Treatment

Most patients who are alert and otherwise well may be treated with oral therapy to lower BP gradually.

First-line treatment should be with a β-blocker (unless contraindicated) with a thiazide diuretic, or a low-dose calcium antagonist.

Urgent invasive monitoring (arterial line) prior to drug therapy is indicated for patients with the following:

- Evidence of hypertensive encephalopathy
- Complications of hypertension (e.g., aortic dissection, acute pulmonary edema or renal failure)
- Treatment of underlying condition (e.g., glomerulonephritis, pheochromocytoma, CREST crisis)
- Patients with persistent diastolic BP ≥140 mmHg
- Eclampsia

Sublingual nifedipine must be avoided.

Conditions requiring specific treatment

See Box 1.4.

Long-term management

- Investigate as appropriate for an underlying cause.
- Select a treatment regime that is tolerated and effective. Tell the patient why long-term therapy is important.
- Try to reduce all cardiovascular risk factors by advising the patient to stop smoking (if applicable), giving appropriate dietary advice (cholesterol), and aiming for optimal diabetic control.
- Monitor long-term control and look for end-organ damage (regular fundoscopy, ECG, blood work). Even poor control is better than no control.

Box 1.4 Conditions requiring specific treatment

- Accelerated and malignant hypertension
- Hypertensive encephalopathy
- Eclampsia
- Pheochromocytoma
- Hypertensive patients undergoing anesthesia

Drugs for hypertensive emergencies

Table 1.4 Drugs for treatment of hypertensive emergencies: IV therapy

Drug	Dosage	Onset of action	Comments
Labetalol	20–80 mg IV bolus q10min 20–200 mg/min by IV infusion, increasing every 15 minutes	2–5 minutes	Drug of choice in suspected pheochromocytoma or aortic dissection. Avoid if there is LVF. May be continued orally (see below)
Nitroprusside	0.25–10 μg/kg/min IV infusion	Seconds	Drug of choice in LVF and/or encephalopathy
Nitroglycerine	1–10 mg/hr IV infusion	2–5 minutes	Mainly venodilatation. Useful in patients with LVF or angina
Hydralazine	5–10 mg IV over 20 minutes 50–300 μg/min IV infusion	10–15 minutes	May provoke angina
Esmolol HCl	500 μg/kg/min IV loading dose 50–200 μg/kg/min IV infusion	Seconds	Short-acting β-blocker also used for SVTs
Phentolamine	2–5 mg IV over 2–5 minutes prn	Seconds	

NB: It is dangerous to reduce the blood pressure quickly. Aim to reduce DBP to 100–110 mmHg within 2–4 hours. Unless there are good reasons to commence IV therapy, always use oral medicines.

Table 1.5 Drugs for treatment of hypertensive emergencies: oral therapy

Drug	Dosage	Onset of action	Comment
Atenolol	50–100 mg po daily	30–60 minutes	There are numerous alternative β-blockers
Nimodipine	10–20 mg po q8h (q12h if slow release)	15–20 minutes	Avoid sublingual use, as the fall in BP is very rapid
Labetalol	100–400 mg po q12h	30–60 minutes	Use if pheochromocytoma suspected. Safe in pregnancy
Hydralazine	10–50 mg po q8h	20–40 minutes	Safe in pregnancy
Minoxidil	5–10 mg po od	30–60 minutes	May cause marked salt and water retention Combine with a loop diuretic (e.g., furosemide 40–240 mg daily)
Clonidine	0.2 mg po followed by 0.1 mg hourly max. 30–60 minutes 0.8 mg total for urgent therapy, or 0.05–0.1 mg po q8h increasing every 2 days	30–60 minutes	Sedation is common. Do not stop abruptly as here is a high incidence of rebound hypertensive crisis

Note: Aim to reduce DBP to 100–110 mmHg in 2–4 hours and normalize BP in 2–3 days.