Handbook of Drugs in Intensive Care

An A–Z Guide

Third Edition

Henry Paw and Gilbert Park

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A thoroughly updated edition of this well-established guide to drugs and prescribing for intensive care. The book is split into two sections: an A–Z guide to the drugs available, and concise notes on the key topics and situations faced on a daily basis. The A-Z section provides succinct information on each drug including uses, limitations, administration directions and adverse effects. The second section details complications that may arise in patients with particular conditions such as diabetes, epilepsy and renal failure, and other factors that may affect drug prescribing. There is also a section of key data, showing weight conversions, body mass index and corresponding dosage calculations. This edition includes a colour fold-out chart showing drug compatibility for intravenous administration. Presented in a concise, compact format, this book is an invaluable resource for doctors, nurses and other medical professionals caring for critically ill patients.

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This book is dedicated to Georgina Paw

Handbook of Drugs in Intensive Care: An A-Z Guide

3rd ed

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INTRODUCTION

The main challenge when I embarked in writing the third edition has been to keep it down to size. This third edition remains a concise book that explains how to use drugs safely and effectively in a critical care setting. Doctors, nurses and other professionals caring for the critically ill patient will find it useful. It is intended to be small enough to fit in the pocket and to provide sufficient information about drug prescribing in the critically ill patient. To keep the book down to size has meant restricting the list of drugs to ones that I consider as common drugs. It is not intended to list every conceivable complication and problem that can occur with a drug but to concentrate on those the clinician is likely to encounter. These constraints mean that this pocket book should be seen as complementary to, rather than replacing, the standard textbooks.

The book is composed of two main sections. The A-Z guide is the major part and is arranged alphabetically by the non-proprietary name of the drug. This format has made it easier for the user to find a particular drug when in a hurry. The discussion on an individual drug is restricted to its use in the critically ill adult patient. The second part is comprised of short notes on relevant intensive care topics.

While every effort has been made to check drug dosages based on a 70 kg adult and information about every drug, it is still possible that errors may have crept in. I would therefore ask readers to check the information if it seems incorrect. In addition, I would be pleased to hear from any readers with suggestions about how this book can be improved. Comments should be sent via e-mail to: henry.paw@york.nhs.uk.

HGWP
York 2006

HOW TO USE THIS BOOK

European law (directive 92/27/EEC) requires the use of the Recommended International Non-proprietary Name (rINN) in place of the British Approved Name (BAN). For a small number of drugs these names are different. The Department of Health requires the use of BAN to cease and be replaced by rINN with the exceptions of adrenaline and noradrenaline. For these two drugs both their BAN and rINN will continue to be used.

The format of this book was chosen to make it more 'user friendly' – allowing the information to be readily available to the reader in times of need. For each drug there is a brief introduction, followed by the following categories:

Uses
This is the indication for the drug's use in the critically ill. There will be some unlicensed use included and this will be indicated in brackets.

Contraindications
This includes conditions or circumstances in which the drug should not be used – the contraindications. For every drug, this includes known hypersensitivity to the particular drug or its constituents.

Administration
This includes the route and dosage for a 70 kg adult. For obese patients, estimated ideal body weight should be used in the calculation of the dosage (Appendix D). It also advises on dilutions and situations where dosage may have to be modified. To make up a dilution, the instruction 'made up to 50 ml with 0.9% saline' means that the final volume is 50 ml. In contrast, the instruction 'to dilute with 50 ml 0.9% saline' could result in a total volume >50 ml. It is recommended that no drug should be stored for >24 h after reconstitution or dilution.

How not to use . . .
Describes administration techniques or solutions for dilution which are not recommended.

Adverse effects
These are effects other than those desired.

Cautions
Warns of situations when the use of the drug is not contraindicated but needs to be carefully watched. This will include drug–drug interactions.

Organ failure
Highlights any specific problems that may occur when using the drug in a particular organ failure.

Renal replacement therapy
Provides guidance on the effects of haemofiltration/dialysis on the handling of the drug. For some drugs, data are either limited or not available.

ABBREVIATIONS

ACE-I	angiotensin converting enzyme inhibitor
ACh	acetylcholine
ACT	activated clotting time
ADH	antidiuretic hormone
AF	atrial fibrillation
APTT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
AV	atrioventricular
BP	blood pressure
CABG	coronary artery bypass graft
cAMP	cyclic AMP
CC	creatinine clearance
CMV	cytomegalovirus
CNS	central nervous system
CO	cardiac output
COPD	chronic obstructive pulmonary disease
CPR	cardiopulmonary resuscitation
CSF	cerebrospinal fluid
CT	computerised tomography
CVVH	continuous veno-venous haemofiltration
CVVHD	continuous veno-venous haemodiafiltration
DI	diabetes insipidus
DIC	disseminated intravascular coagulation
DVT	deep vein thrombosis
EBV	Epstein Barr virus
ECG	electrocardiogram
EEG	electroencephalogram
EMD	electromechanical dissociation
$ETCO_2$	end-tidal carbon dioxide concentration
FBC	full blood count
FFP	fresh frozen plasma
g	gram
GFR	glomerular filtration rate
GI	gastrointestinal
HOCM	hypertrophic obstructive cardiomyopathy
h	hour
HR	heart rate
ICP	intracranial pressure
ICU	intensive care unit
IHD	ischaemic heart disease
IM	intramuscular
INR	international normalised ratio
IOP	intraocular pressure
IPPV	intermittent positive pressure ventilation
IV	intravenous
K^+	potassium
kg	kilogram

l	litre
LFT	liver function tests
LMWH	low molecular weight heparin
MAOI	monoamine oxidase inhibitor
M6G	morphine-6-glucuronide
mg	milligram
MH	malignant hyperthermia
MI	myocardial infarction
MIC	minimum inhibitory concentration
min	minute
ml	millilitre
MRSA	methicillin-resistant *Staphylococcus aureus*
NG	nasogastric route
ng	nanogram
NJ	nasojejunal
nocte	at night
NSAID	non-steroidal anti-inflammatory drugs
PaO_2	partial pressure of oxygen in arterial blood
$PaCO_2$	partial pressure of carbon dioxide in arterial blood
PCAS	patient controlled analgesia system
PCP	*Pneumocystis carinii* pneumonia
PCWP	pulmonary capillary wedge pressure
PD	peritoneal dialysis
PE	pulmonary embolism
PEA	pulseless electrical activity
PEG	percutaneous endoscopic gastrostomy
PEJ	percutaneous endoscopic jejunostomy
PO	*per orum* (by mouth)
PR	*per rectum* (rectal route)
PRN	*pro re nata* (as required)
PVC	polyvinyl chloride
PVD	peripheral vascular disease
s	second
SC	subcutaneous
SIRS	systemic inflammatory response syndrome
SL	sublingual
SSRI	selective serotonin re-uptake inhibitors
SVR	systemic vascular resistance
SVT	supraventricular tachycardia
TFT	thyroid function tests
TNF	tumour necrosis factor
TPN	total parenteral nutrition
U&E	urea and electrolytes
VF	ventricular fibrillation
VRE	Vancomycin-resistant *Enterococcus faecium*
VT	ventricular tachycardia
WFI	water for injection
WPW syndrome	Wolff-Parkinson-White syndrome

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I would like to thank all my colleagues from whom I have sought advice during the preparation of this book. In particular, I acknowledge the assistance of Dr Neil Todd for microbiological advice.

Drugs:
An A–Z Guide

ACETAZOLAMIDE

Acetazolamide is a carbonic anhydrase inhibitor normally used to reduce intra-ocular pressure in glaucoma. Metabolic alkalosis may be partially corrected by the use of acetazolamide. The most common cause of metabolic alkalosis on the ICU is usually the result of furosemide administration.

Uses
Metabolic alkalosis (unlicensed)

Contraindications
Hypokalaemia
Hyponatraemia
Hyperchloraemic acidosis
Severe liver failure
Renal failure
Sulphonamide hypersensitivity

Administration
- IV: 250–500 mg, given over 3–5 min every 8 hours

Reconstitute with 5 ml WFI
Monitor: FBC, U&E and acid/base balance

How not to use acetazolamide
IM injection – painful
Not for prolonged use

Adverse effects
Metabolic acidosis
Electrolyte disturbances (hypokalaemia and hyponatraemia)
Blood disorders
Abnormal LFT

Cautions
Avoid extravasation at injection site (risk of necrosis)
Avoid prolonged use (risk of adverse effects)
Concurrent use with phenytoin (↑ serum level of phenytoin)

Organ failure
Renal: avoid (metabolic acidosis)
Hepatic: avoid (abnormal LFT)

ACETYLCYSTEINE (Parvolex)

Acetylcysteine is an effective antidote to paracetamol if administered within 8 h after an overdose. Although the protective effect diminishes progressively as the overdose – treatment interval increases, acetylcysteine can still be of benefit up to 24 h after the overdose. In paracetamol overdose the hepatotoxicity is due to formation of a toxic metabolite. Hepatic reduced glutathione inactivates the toxic metabolite by conjugation, but glutathione stores are depleted with hepatotoxic doses of paracetamol. Acetylcysteine, being a sulphydryl (SH) group donor, protects the liver probably by restoring depleted hepatic reduced glutathione or by acting as an alternative substrate for the toxic metabolite.

Acetylcysteine may have significant cytoprotective effects. The cellular damage associated with sepsis, trauma, burns, pancreatitis, hepatic failure and tissue reperfusion following acute MI may be mediated by the formation and release of large quantities of free radicals that overwhelm and deplete endogenous antioxidants (e.g. glutathione). Acetylcysteine is a scavenger of oxygen free radicals. In addition, acetylcysteine is a glutathione precursor capable of replenishing depleted intracellular glutathione and in theory augment antioxidant defences (p. 222).

Nebulized acetylcysteine can be used as a mucolytic agent. It reduces sputum viscosity by disrupting the disulphide bonds in the mucus glycoproteins and enhances mucociliary clearance, thus facilitating easier expectoration.

Uses
Paracetamol overdose
Antioxidant (unlicensed)
Reduce sputum viscosity and facilitate easier expectoration (unlicensed)
As a sulphydryl group donor to prevent the development of nitrate tolerance (unlicensed)

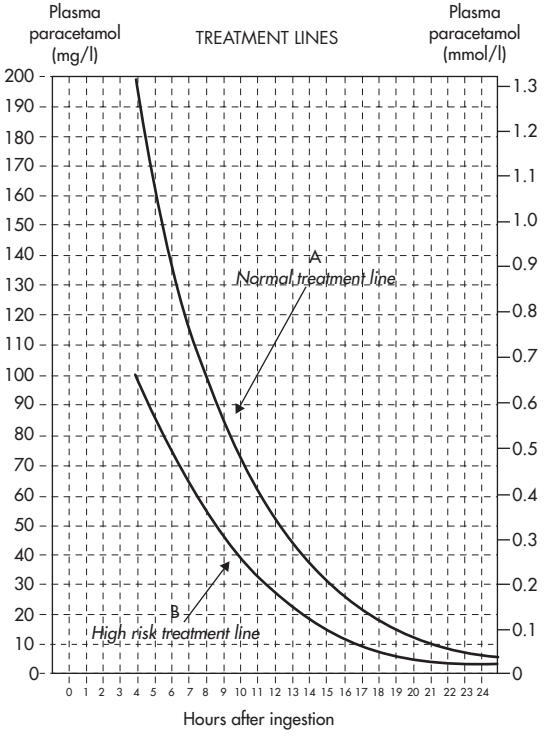
Administration
Paracetamol overdose

- IV infusion: 150 mg/kg in 200 ml 5% dextrose over 15 min, followed by 50 mg/kg in 500 ml 5% dextrose over 4 h, then 100 mg/kg in 1 litre 5% dextrose over the next 16 h

Weight (kg)	Initial	Second	Third
	150 mg/kg in 200 ml 5% dextrose over 15 min	50 mg/kg in 500 ml 5% dextrose over 4 h	100 mg/kg in 1 litre 5% dextrose over 16 h
	Parvolex (ml)	Parvolex (ml)	Parvolex (ml)
50	37.5	12.5	25
60	45.0	15.0	30
70	52.5	17.5	35
80	60.0	20.0	40
90	67.5	22.5	45
x	0.75x	0.25x	0.5x

For children >20 kg: same doses and regimen but in half the quantity of IV fluid

Treatment nomogram



Patients whose plasma concentrations fall on or above treatment line A should receive acetylcysteine. Patients with induced hepatic microsomal oxidase enzymes (for chronic alcoholics and patients taking enzyme-inducing drugs, see p. 191) are susceptible to paracetamol-induced hepatotoxicity at lower paracetamol concentrations and should be assessed against treatment line B.

Antioxidant

- IV infusion: 75–100 mg/kg in 1 litre 5% dextrose, give over 24 h (rate 40 ml/h)

Reduce sputum viscosity

- Nebulized: 4 ml 800 mg undiluted Parvolex (20%) driven by air, 8 hourly

Administer before chest physiotherapy

How not to use acetylcysteine
Do not drive nebulizer with oxygen (oxygen inactivates acetylcysteine)

Adverse effects
Anaphylactoid reactions (nausea, vomiting, flushing, itching, rashes, bronchospasm, hypotension)
Fluid overload

Cautions
Asthmatics (risk of bronchospasm)
Pulmonary oedema (worsens)
Each 10 ml ampoule contains Na^+ 12.78 mmol (↑ total body sodium)

ACICLOVIR (Zovirax)

Interferes with herpes virus DNA polymerase, inhibiting viral DNA replication. Aciclovir is renally excreted and has a prolonged half-life in renal impairment.

Uses
Herpes simplex virus infections:

- HSV encephalitis
- HSV genital, labial, peri-anal and rectal infections

Varicella zoster virus infections:

- Beneficial in the immunocompromised patients when given IV within 72 h: prevents complications of pneumonitis, hepatitis or thrombocytopenia
- In patients with normal immunity, may be considered if the ophthalmic branch of the trigeminal nerve is involved

Contraindications
Not suitable for CMV or EBV infections

Administration
- IV: 5–10 mg/kg 8 hourly

Available in 250 and 500 mg vials for reconstitution
Reconstitute 250 mg vial with 10 ml WFI or 0.9% saline (25 mg/ml)
Reconstitute 500 mg vial with 20 ml WFI or 0.9% saline (25 mg/ml)
Take the reconstituted solution (25 mg/ml) and make up to 50 ml (for 250 mg vial) or 100 ml (for 500 mg vial) with 0.9% saline or 5% dextrose, and give over 1 h
Ensure patient is well hydrated before treatment is administered
In renal impairment:

CC (ml/min)	Dose (mg/kg)	Interval (h)
10–20	5	12
<10	2.5	24

How not to use aciclovir
- Rapid IV infusion (precipitation of drug in renal tubules leading to renal impairment)

Adverse effects
Phlebitis
Reversible renal failure
Elevated liver function tests
CNS toxicity (tremors, confusion and fits)

Cautions
Concurrent use of methotrexate
Renal impairment (reduce dose)
Dehydration/hypovolaemia (renal impairment due to precipitation in renal tubules)

Renal replacement therapy
Removed by HD and HF, similar to urea clearance. Elimination will only be significant for high clearance systems. Dose as for CC 10–25 ml/min. Not significantly cleared by PD.

ADENOSINE (Adenocor)

This endogenous nucleoside is safe and effective in ending >90% of re-entrant paroxysmal SVT. However, this is not the most common type of SVT in the critically ill patient. After an IV bolus effects are immediate (10–30 s), dose-related and transient (half-life <10 s; entirely eliminated from plasma in <1 min, being degraded by vascular endothelium and erythrocytes). Its elimination is not affected by renal/hepatic disease. Adenosine works faster and is superior to verapamil. It may be used in cardiac failure, in hypotension, and with β-blockers, in all of which verapamil is contraindicated.

Uses
It has both therapeutic and diagnostic uses:

- Alternative to DC cardioversion in terminating paroxysmal SVT, including those associated with WPW syndrome
- Determining the origin of broad complex tachycardia; SVT responds, VT does not (predictive accuracy 92%; partly because VT may occasionally respond). Though adenosine does no harm in VT, verapamil may produce hypotension or cardiac arrest

Contraindications
Second- or third-degree heart block (unless pacemaker fitted)
Sick sinus syndrome (unless pacemaker fitted)
Asthmatic – may cause bronchospasm
Patients on dipyridamole (drastically prolongs the half-life and enhances the effects of adenosine – may lead to dangerously prolonged high-degree AV block)

Administration
- Rapid IV bolus: 3mg over 1–2s into a large vein, followed by rapid flushing with 0.9% saline

If no effect within 2 min, give 6 mg
If no effect within 2 min, give 12 mg
If no effect, abandon adenosine
Need continuous ECG monitoring
More effective given via a central vein or into right atrium

How not to use adenosine
Without continuous ECG monitor

Adverse effects
Flushing (18%), dyspnoea (12%), and chest discomfort are the commonest side-effects but are well tolerated and invariably last <1 min. If given to an asthmatic and bronchospasm occurs, this may last up to 30 min (use aminophylline to reverse).

Cautions

AF or atrial flutter with accessory pathway (↑ conduction down anomalous pathway may increase)

Early relapse of paroxysmal SVT is more common than with verapamil but usually responds to further doses

Adenosine's effect is enhanced and extended by dipyridamole – if essential to give with dipyridamole, reduce initial dose to 0.5–1.0 mg

ADRENALINE

Both α- and β-adrenergic receptors are stimulated. Low doses tend to produce predominantly β-effects while higher doses tend to produce predominantly α-effects. Stimulation of β_1-receptors in the heart increases the rate and force of contraction, resulting in an increase in cardiac output. Stimulation of α_1-receptor causes peripheral vasoconstriction, which increases the systolic BP. Stimulation of β_2-receptors causes bronchodilatation and vasodilatation in certain vascular beds (skeletal muscles). Consequently, total systemic resistance may actually fall, explaining the decrease in diastolic BP that is sometimes seen.

Uses
Low cardiac output states
Cardiac arrest (p. 198)
Anaphylaxis (p. 200)

Contraindications
Before adequate intravascular volume replacement

Administration
Low cardiac output states
Dose: 0.01–0.30 mcg/kg/min IV infusion via a central vein
Titrate dose according to HR, BP, cardiac output, presence of ectopic beats and urine output
4 mg made up to 50 ml 5% dextrose

Dosage chart (ml/h)

Weight (kg)	Dose (mcg/kg/min)				
	0.02	0.05	0.1	0.15	0.2
50	0.8	1.9	3.8	5.6	7.5
60	0.9	2.3	4.5	6.8	9.0
70	1.1	2.6	5.3	7.9	10.5
80	1.2	3.0	6.0	9.0	12
90	1.4	3.4	6.8	10.1	13.5
100	1.5	3.8	7.5	11.3	15.0
110	1.7	4.1	8.3	12.4	16.5
120	1.8	4.5	9.0	13.5	18.0

Cardiac arrest (p. 198)

- IV bolus: 10 ml 1 in 10 000 solution (1 mg).

Anaphylaxis (p. 200)

- IV bolus: 0.5–1.0 ml 1 in 10 000 solution (50–100 mcg), may be repeated PRN, according to BP

How not to use adrenaline
In the absence of haemodynamic monitoring
Do not connect to CVP lumen used for monitoring pressure (surge of drug during flushing of line)
Incompatible with alkaline solutions, e.g. sodium bicarbonate, frusemide, phenytoin and enoximone

Adverse effects
Arrhythmia
Tachycardia
Hypertension
Myocardial ischaemia

Cautions
Acute myocardial ischaemia or MI

ALFENTANIL

It is 30 times more potent than morphine and its duration is shorter than that of fentanyl. The maximum effect occurs about 1 min after IV injection. Duration of action following an IV bolus is between 5 and 10 min. Its distribution volume and lipophilicity are lower than fentanyl. It is ideal for infusion and may be the agent of choice in renal failure. The context sensitive half-life may be prolonged following IV infusion. In patients with hepatic failure the elimination half-life may be markedly increased and a prolonged duration of action may be seen.

Uses
Patients receiving short-term ventilation

Contraindications
Airway obstruction
Concomitant use of MAOI

Administration
- IV bolus: 500 mcg every 10 min as necessary
- IV infusion rate: 1–5 mg/h (up to 1 mcg/kg/min)

How not to use alfentanil
In combination with an opioid partial agonist, e.g. buprenorphine (antagonizes opioid effects)

Adverse effects
Respiratory depression and apnoea
Bradycardia
Nausea and vomiting
Delayed gastric emptying
Reduce intestinal mobility
Biliary spasm
Constipation
Urinary retention
Chest wall rigidity (may interfere with ventilation)

Cautions
Enhanced sedative and respiratory depression from interaction with:

- benzodiazepines
- antidepressants
- anti-psychotics

Avoid concomitant use of and for 2 weeks after MAOI discontinued (risk of CNS excitation or depression – hypertension, hyperpyrexia, convulsions and coma)

Head injury and neurosurgical patients (may exacerbate ↑ ICP as a result of ↑ $PaCO_2$)
Erythromycin (↓ clearance of alfentanil)

Organ failure
Respiratory: ↑ respiratory depression
Hepatic: enhanced and prolonged sedative effect