

THE COMPLETE

Vasopressor & Inotrope Handbook

A Practical Guide for Healthcare Professionals

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The Complete Vasopressor & Inotrope Handbook: A Practical Guide for Healthcare Professionals

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Published by Klinix Creation

ISBN (paperback): 9789403950648

First edition, 2026. Content current to the literature available in October 2026.

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Medical Disclaimer

This handbook is an educational resource written for physicians, advanced practice providers, pharmacists, nurses, respiratory therapists, and trainees who care for patients with circulatory failure. It is not a substitute for clinical judgment, institutional protocols, product labeling, or consultation with appropriate specialists.

Vasoactive drugs are high-alert medications. Doses, concentrations, and administration practices vary between countries, hospitals, and product formulations, and a single decimal-point error can cause serious harm. Before prescribing, preparing, or administering any agent discussed here, verify the dose against current prescribing information, your institution's protocols, and a pharmacist where possible.

The evidence summarized in this book reflects the published literature and guidelines available at the time of writing. Medicine changes quickly; trials are published, guidelines are revised, and drugs are approved, withdrawn, or relabeled. Readers are responsible for confirming that the information they rely on remains current.

Where the evidence is uncertain, this book says so. Statements labeled as practical approaches or common practice describe how clinicians frequently manage a problem; they are not guideline recommendations unless a guideline is cited.

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Case scenarios in this book are composites written for teaching. They do not describe real patients, and any resemblance to an actual person is coincidental.

For the Reader

For the night-shift nurse who notices the pressure drifting before the alarm sounds, the pharmacist who catches the misplaced decimal, the resident standing alone at the bedside at 3 a.m., and every clinician who has ever had to decide, quickly and without certainty, what a failing circulation needs next.

This book is written for you.

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How to Use This Book

This handbook is organized around the questions clinicians actually ask at the bedside. Each chapter opens with the physiology you need, moves quickly to the decisions you will face, and closes with the points worth remembering. You can read it from cover to cover as a course, or open it to a single chapter when a specific drug or problem is in front of you.

Five recurring features appear throughout the text:

> **Clinical Pearl.** A practical observation that sharpens bedside decision-making.

> **Pitfall.** A common error, misconception, or safety hazard, and how to avoid it.

> **Evidence Check.** A concise summary of the key trial or guideline behind a recommendation.

> **Gray Zone.** An area where evidence is limited or experts disagree. Treat these as prompts for judgment, not as rules.

> **Bottom Line.** The essential take-home messages at the end of each chapter.

On doses. Dose ranges are provided because a handbook without them is of limited practical use. They are typical adult ranges drawn from product labeling, guidelines, and pivotal trials. They are not orders. Always confirm doses, concentrations, and units against your local protocols.

On units. Some institutions dose catecholamines by weight (mcg/kg/min) and others by fixed rate (mcg/min). This book generally uses weight-based units and gives approximate fixed-rate equivalents for a 70-kg adult where helpful. Chapter 2 explains why mixing the two systems is a recurring source of error.

On citations. Superscript numbers refer to the numbered reference list at the end of the book. Primary trials and guidelines are cited so that you can read the original sources and form your own view.

Key Abbreviations

Abbreviations used throughout this book

Abbreviation	Meaning
AKI	Acute kidney injury
cAMP / cGMP	Cyclic adenosine / guanosine monophosphate
CI	Cardiac index (L/min/m²)
CO	Cardiac output (L/min)
CPO	Cardiac power output (W)
CRT	Capillary refill time
CVP	Central venous pressure
DBP / SBP	Diastolic / systolic blood pressure
DO_2	Oxygen delivery
ECMO	Extracorporeal membrane oxygenation
G6PD	Glucose-6-phosphate dehydrogenase
LVOT VTI	Left ventricular outflow tract velocity–time integral
MAP	Mean arterial pressure
MCS	Mechanical circulatory support
NE	Norepinephrine
NEE	Norepinephrine equivalent dose
NO	Nitric oxide
PAC	Pulmonary artery catheter
PAPi	Pulmonary artery pulsatility index
PCWP	Pulmonary capillary wedge pressure
PDE3	Phosphodiesterase-3
PLR	Passive leg raise
RAP	Right atrial pressure
RV / LV	Right / left ventricle
SCAI	Society for Cardiovascular Angiography and Interventions
$ScvO_2$ / SvO_2	Central / mixed venous oxygen saturation
SSC	Surviving Sepsis Campaign
SVR	Systemic vascular resistance
V1 / V2	Vasopressin receptor subtypes 1 and 2

BEFORE YOU BEGIN

Introduction

Why another book on vasoactive drugs?

Few decisions in acute care are made as quickly, or with as much consequence, as the decision to start a vasopressor or inotrope. The drugs act within minutes, their effects can reverse just as quickly, and the margin between help and harm is narrow. A patient may receive three or four vasoactive agents in a single day, each chosen by a different clinician, each titrated by a nurse responding to a number on a monitor.

Yet many clinicians learn these drugs piecemeal: a receptor table memorized for an examination, a dosing chart taped to an infusion pump, a habit inherited from the last attending physician. The result is often a working knowledge that is adequate on an ordinary shift but brittle when a patient fails to respond as expected.

This handbook aims to replace that piecemeal knowledge with a coherent framework. It is deliberately compact. It is not a pharmacology textbook, and it does not try to catalog every study ever performed. Instead it concentrates on the physiology, evidence, and practical judgment that matter most when a real patient's circulation is failing.

The five bedside questions

Every chapter in this book returns, directly or indirectly, to five questions. They form a mental checklist that applies to any patient in shock and any vasoactive drug.

1. What is failing: pressure, flow, or both? Hypotension and hypoperfusion are related but not identical. A patient can have a normal blood pressure with inadequate cardiac output, or a low pressure with ample flow. The right drug depends on which problem dominates.

2. Why is it failing? Vasodilation, pump failure, inadequate volume, and obstruction each call for different treatment. Vasoactive drugs buy time; they rarely fix the cause.

3. What will this drug do to pressure, flow, heart rate, and the organs I am trying to protect? Every agent has a receptor profile, and every receptor has consequences beyond the one you intended.

4. How will I know it is working? A rising number on the monitor is necessary but not sufficient. Perfusion markers, organ function, and the trajectory of the patient matter more than any single pressure reading.

5. When and how will I stop? Every infusion started should have an exit plan. The longer and higher the exposure, the greater the cumulative risk.

How this book is organized

Part I builds the foundation: the physiology of shock, receptor pharmacology, and the targets and monitoring tools used to guide therapy.

Part II covers the vasopressors one at a time: norepinephrine, epinephrine, vasopressin and its analogues, phenylephrine, dopamine, and angiotensin II.

Part III turns to drugs that primarily augment cardiac performance: dobutamine, milrinone, levosimendan, and isoproterenol.

Part IV addresses rescue and adjunctive therapies, including corticosteroids, methylene blue, hydroxocobalamin, and oral midodrine.

Part V brings everything together at the bedside: safe administration, peripheral infusions and extravasation, building a regimen in mixed and refractory shock, shock in special settings, peri-intubation and perioperative hypotension, fourteen worked case scenarios, a quick-reference section designed for use on the unit, and a forty-question self-assessment review.

A note on evidence and uncertainty

The evidence base for vasoactive therapy is uneven. A handful of large, well-conducted randomized trials have shaped practice: comparisons of dopamine and norepinephrine, of vasopressin added early or late, of higher and lower blood-pressure targets, and of fluid strategies. Many other everyday decisions, such as when to add a second vasopressor, which agent to wean first, or how to dose an inotrope in mixed shock, rest on physiology, observational data, and expert opinion.

This book tries to be honest about that difference. Where a recommendation comes from a guideline, the guideline is named along with its strength. Where a practice is common but unproven, it is labeled as such. Where reasonable experts disagree, the Gray Zone boxes lay out the competing views.

The 2026 update of the Surviving Sepsis Campaign guidelines,[1] the 2025 American College of Cardiology concise clinical guidance on cardiogenic shock,[2] and several recent randomized trials have changed parts of this field. The text reflects those changes. It also reflects a broader shift in thinking: away from chasing a single blood-pressure number and toward individualized, perfusion-guided care that minimizes unnecessary exposure to vasoactive drugs.

Who this book is for

The intended audience is broad: intensivists and emergency physicians, hospitalists and anesthesiologists, cardiologists, critical care pharmacists, nurses, advanced practice providers, and trainees in all of these fields. Some readers will want the physiology; others will want the dose table. Both are here, and the chapters are written so that each can be read independently. As a result, a few key concepts are deliberately repeated where they matter most.

If this handbook helps you make one safer decision, anticipate one complication, or explain one plan more clearly to a colleague, it will have done its job.

PART I

Foundations

The physiology, pharmacology, and monitoring principles that underpin every decision about vasoactive therapy.

CHAPTER 1

Shock at the Bedside

Pressure, flow, and the failing circulation

What shock is, and what it is not

Q What is the most useful working definition of shock?

Shock is a state in which the circulation fails to deliver enough oxygen to meet the metabolic needs of the tissues, or in which the tissues cannot use the oxygen they receive. The result is cellular dysoxia, a shift toward anaerobic metabolism, and, if uncorrected, progressive organ failure.[3,4] In sepsis specifically, septic shock is defined as sepsis requiring vasopressors to maintain a MAP of 65 mm Hg or more with a serum lactate above 2 mmol/L despite adequate volume resuscitation.[5]

Notice what this definition leaves out: blood pressure. Hypotension is the most common way shock announces itself, but it is a sign, not the disease. A young patient with hemorrhage may maintain a normal systolic pressure through intense vasoconstriction until a large fraction of blood volume is gone. A patient with chronic hypertension may be hypoperfused at a pressure that would be perfectly adequate for someone else. Conversely, a patient under general anesthesia may be hypotensive yet well perfused.

> **CLINICAL PEARL**
>
> Treat hypoperfusion, not just hypotension. A normal blood pressure does not exclude shock, and a low blood pressure does not prove it. Look at the patient: mentation, skin, capillary refill, urine output, and lactate trajectory.

Q How do the four classic categories of shock help at the bedside?

The traditional classification divides shock into four mechanisms:

- **Distributive:** loss of vascular tone, as in sepsis, anaphylaxis, spinal cord injury, and vasoplegia after cardiac surgery.
- **Cardiogenic:** pump failure from myocardial infarction, myocarditis, decompensated cardiomyopathy, arrhythmia, or valvular disease.

- **Hypovolemic:** loss of circulating volume from hemorrhage, vomiting, diarrhea, burns, or third-spacing.
- **Obstructive:** mechanical impediment to flow, as in massive pulmonary embolism, tension pneumothorax, or cardiac tamponade.

The classification is useful because each mechanism has a characteristic hemodynamic fingerprint (Table 1.1) and a different primary treatment. Its limitation is that real patients often have more than one mechanism. Septic shock frequently includes a hypovolemic phase before resuscitation and a cardiogenic component from septic cardiomyopathy. Cardiogenic shock after myocardial infarction can develop a vasodilatory component as systemic inflammation evolves. Thinking in terms of "dominant mechanism plus contributors" is more accurate than forcing a single label.

Table 1.1 Typical hemodynamic profiles of the four shock mechanisms

Mechanism	Cardiac output	SVR	Filling pressures	Venous O_2 saturation
Distributive	Normal or high*	Low	Low to normal	Normal or high
Cardiogenic	Low	High	High	Low
Hypovolemic	Low	High	Low	Low
Obstructive	Low	High	High (RAP)†	Low

**Cardiac output may be low before volume resuscitation or with septic cardiomyopathy. †In pulmonary embolism and tamponade, right-sided pressures rise; in tamponade, pressures tend to equalize across chambers.*

The equation that organizes everything

Q Why is "MAP = CO × SVR" so useful, and where does it mislead?

Blood flow through any vascular bed obeys a relationship analogous to Ohm's law: the pressure drop across the bed equals flow multiplied by resistance. For the systemic circulation, the pressure drop is the mean arterial pressure minus the right atrial pressure, so:

MAP − RAP = CO × SVR

Because RAP is usually small relative to MAP, the bedside shorthand becomes MAP ≈ CO × SVR. This simple relationship tells you that a low blood pressure must result from low flow, low resistance, or both. It also tells you how each drug class works: vasopressors raise SVR, inotropes raise CO, and many agents do some of each.

The equation has two important limitations. First, SVR is not measured directly; it is calculated from MAP, RAP, and CO, so any error in those values propagates into the result. Second, a rise in MAP does not mean that flow improved. If a vasopressor raises SVR while cardiac output falls, MAP may rise while tissue perfusion worsens. This is the central hazard of excessive vasoconstriction, especially in a weak heart.

> **PITFALL**
> A higher MAP is not automatically better perfusion. When pressure rises but lactate, mentation, urine output, and capillary refill do not improve, consider whether you have raised resistance at the expense of flow.

Q What determines cardiac output?

Cardiac output is the product of heart rate and stroke volume. Stroke volume, in turn, depends on three factors:

- **Preload:** ventricular filling at end-diastole, determined largely by venous return.
- **Contractility:** the intrinsic force of contraction at a given preload.
- **Afterload:** the load the ventricle must overcome to eject, reflected in arterial pressure and vascular impedance.

The normal left ventricle tolerates a wide range of afterload with little change in stroke volume. The failing ventricle does not; its stroke volume falls steeply as afterload rises. The right ventricle is even more sensitive to its afterload, the pulmonary vascular resistance. These differences explain why a pure vasoconstrictor may be well tolerated in septic shock with a vigorous heart, yet harmful in a patient with severe systolic dysfunction.

Venous return: the forgotten half of the circulation

Q How can a vasopressor increase cardiac output?

This surprises many clinicians. About 70% of blood volume sits in the veins, especially in the splanchnic circulation. Most of this volume is "unstressed": it fills the veins without stretching them and does not generate pressure. A smaller "stressed" volume stretches the vessel walls and creates the mean systemic filling pressure, which drives blood back toward the heart.

Alpha-adrenergic agonists constrict veins as well as arteries. Venoconstriction shifts blood from the unstressed to the stressed compartment, increasing the pressure gradient for venous return. In a patient whose heart can respond to more preload, cardiac output rises. This is one reason norepinephrine often increases cardiac output in early septic shock, and why starting a vasopressor early can reduce the volume of fluid needed to restore pressure.[6]

The flip side is that the same drug raises arterial resistance. Whether cardiac output rises or falls depends on the balance between increased venous return and increased afterload, which in turn depends on the state of the heart and the volume status of the patient.

> **CLINICAL PEARL**
>
> In a hypotensive, vasodilated patient with a good ventricle, norepinephrine often acts as an "internal fluid bolus" by mobilizing unstressed venous volume. In a patient with a failing ventricle, the afterload effect may dominate instead.

Perfusion pressure and autoregulation

Q Why does the MAP target matter for specific organs?

Each organ is perfused by the difference between the arterial pressure entering it and the pressure opposing flow out of it. For most organs, that opposing pressure is venous pressure; for the brain, it is intracranial pressure; for the abdominal organs, it may be intra-abdominal pressure.

- **Kidney:** renal perfusion pressure is approximately MAP minus CVP (or intra-abdominal pressure, whichever is higher). A high CVP from fluid overload or right heart failure reduces renal perfusion as surely as a low MAP does.
- **Brain:** cerebral perfusion pressure is MAP minus intracranial pressure (or CVP if higher).
- **Heart:** the left ventricle is perfused mainly during diastole, so coronary perfusion depends on diastolic arterial pressure minus left ventricular end-diastolic pressure, and on the time spent in diastole.

Most organs autoregulate, holding flow fairly constant across a range of perfusion pressures. Below the lower limit, flow becomes pressure-dependent. Chronic hypertension shifts the autoregulatory curve to the right, so a hypertensive patient may need a higher pressure to maintain the same organ flow. This physiological argument is the basis for