



# The Cardiovascular System at a Glance

**Fourth Edition**

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### **Companion website**

A companion website is available at:

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featuring:

- Case Studies from this and previous editions
- Key points for revision

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# Preface

This book is designed to present a concise description of the cardiovascular system which integrates normal structure and function with pathophysiology, pharmacology and therapeutics. We therefore cover in an accessible yet comprehensive manner all of the topics that preclinical medical students and biomedical science students are likely to encounter when they are learning about the cardiovascular system. However, our aims in writing and revising this book have always been more ambitious – we have also sought to provide to our readers a straightforward description of many fascinating and important topics that are neglected or covered only superficially by many other textbooks and most university and medical courses. We hope that this book will not only inform you about the cardiovascular system, but enthuse you to look more deeply into at least some of its many remarkable aspects.

In addition to making substantial revisions designed to update the topics, address reviewers' criticisms and simplify some of the diagrams, we have added a new chapter on pulmonary hypertension for this fourth edition and written eight entirely new self-assessment case studies, each drawing on encounters with real patients.

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Jeremy P.T. Ward  
Michelle J. Connolly

## Recommended reading

Bonow R.O., Mann D.L., Zipes D.P. & Libby P. (Eds) (2011) *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 9th edition. Elsevier Health Sciences.

Levick J.R. (2010) *An Introduction to Cardiovascular Physiology*, 5th edition. Hodder Arnold.

Lilly L.S. (Ed). (2010) *Pathophysiology of Heart Disease: A Collaborative Project of Medical Students and Faculty*, 5th edition. Lippincott Williams and Wilkins.



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We are grateful to Karen Moore for her assistance in keeping track of our progress, putting up so gracefully with our missed deadlines, and generally making sure that this book and its companion website not only became a reality, but did so on schedule. Finally, as always, we thank our readers, particularly our students at King's College London, whose support over the years has encouraged us to keep trying to make this book better.

# List of abbreviations

<b>5-HT</b>	5-hydroxytryptamine (serotonin)
<b>AAA</b>	abdominal aortic aneurysm
<b>ABP</b>	arterial blood pressure
<b>AC</b>	adenylate cyclase
<b>ACE</b>	angiotensin-converting enzyme
<b>ACEI</b>	angiotensin-converting enzyme inhibitor/s
<b>ACS</b>	acute coronary syndromes
<b>ADH</b>	antidiuretic hormone
<b>ADMA</b>	asymmetrical dimethyl arginine
<b>ADP</b>	adenosine diphosphate
<b>AF</b>	atrial fibrillation
<b>AMP</b>	adenosine monophosphate
<b>ANP</b>	atrial natriuretic peptide
<b>ANS</b>	autonomic nervous system
<b>AP</b>	action potential
<b>APAH</b>	pulmonary hypertension associated with other conditions
<b>APC</b>	active protein C
<b>APD</b>	action potential duration
<b>aPTT</b>	activated partial thromboplastin time
<b>AR</b>	aortic regurgitation
<b>ARB</b>	angiotensin II receptor blocker
<b>ARDS</b>	acute respiratory distress syndrome
<b>AS</b>	aortic stenosis
<b>ASD</b>	atrial septal defect
<b>ATP</b>	adenosine triphosphate
<b>AV</b>	atrioventricular
<b>AVA</b>	arteriovenous anastomosis
<b>AVN</b>	atrioventricular node
<b>AVNRT</b>	atrioventricular nodal re-entrant tachycardia
<b>AVRT</b>	atrioventricular re-entrant tachycardia
<b>BBB</b>	blood-brain barrier
<b>BP</b>	blood pressure

<b>CABG</b>	coronary artery bypass grafting
<b>CAD</b>	coronary artery disease
<b>CaM</b>	calmodulin
<b>cAMP</b>	cyclic adenosine monophosphate
<b>CCB</b>	calcium-channel blocker
<b>CE</b>	cholesteryl ester
<b>CETP</b>	cholesteryl ester transfer protein
<b>CFU-E</b>	colony-forming unit erythroid cell
<b>cGMP</b>	cyclic guanosine monophosphate
<b>CHD</b>	congenital heart disease
<b>CHD</b>	coronary heart disease
<b>CHF</b>	chronic heart failure
<b>CICR</b>	calcium-induced calcium release
<b>CK-MB</b>	creatine kinase MB
<b>CNS</b>	central nervous system
<b>CO</b>	cardiac output
<b>COPD</b>	chronic obstructive pulmonary disease
<b>COX</b>	cyclooxygenase
<b>CPVT</b>	catecholaminergic polymorphic ventricular tachycardia
<b>CRP</b>	C-reactive protein
<b>CSF</b>	cerebrospinal fluid
<b>CT</b>	computed tomography
<b>CTPA</b>	computed tomography pulmonary angiogram
<b>CVD</b>	cardiovascular disease
<b>CVP</b>	central venous pressure
<b>CXR</b>	chest X-ray
<b>DAD</b>	delayed afterdepolarization
<b>DAG</b>	diacylglycerol
<b>DBP</b>	diastolic blood pressure
<b>DC</b>	direct current
<b>DHP</b>	dihydropyridine
<b>DIC</b>	disseminated intravascular coagulation
<b>DM2</b>	type 2 diabetes mellitus
<b>DVT</b>	deep venous/vein thrombosis
<b>EAD</b>	early afterdepolarization
<b>ECF</b>	extracellular fluid

<b>ECG</b>	electrocardiogram/electrocardiograph (EKG)
<b>ECM</b>	extracellular matrix
<b>EDHF</b>	endothelium-derived hyperpolarizing factor
<b>EDP</b>	end-diastolic pressure
<b>EDRF</b>	endothelium-derived relaxing factor
<b>EDTA</b>	ethylenediaminetetraacetic acid
<b>EDV</b>	end-diastolic volume
<b>EET</b>	epoxyeicosatrienoic acid
<b>EnaC</b>	epithelial sodium channel
<b>eNOS</b>	endothelial NOS
<b>ERP</b>	effective refractory period
<b>ESR</b>	erythrocyte sedimentation rate
<b>FDP</b>	fibrin degradation product
<b>GP</b>	glycoprotein
<b>GPI</b>	glycoprotein inhibitor
<b>GTN</b>	glyceryl trinitrate
<b>Hb</b>	haemoglobin
<b>HCM</b>	hypertrophic cardiomyopathy
<b>HDL</b>	high-density lipoprotein
<b>HEET</b>	hydroxyeicosatetraenoic acid
<b>HMG-CoA</b>	hydroxy-methylglutanyl coenzyme A
<b>hPAH</b>	heritable pulmonary arterial hypertension
<b>HPV</b>	hypoxic pulmonary vasoconstriction
<b>HR</b>	heart rate
<b>ICD</b>	implantable cardioverter defibrillator
<b>IDL</b>	intermediate-density lipoprotein
<b>Ig</b>	immunoglobulin
<b>IML</b>	intermediolateral
<b>iNOS</b>	inducible NOS
<b>INR</b>	international normalized ratio
<b>IP<sub>3</sub></b>	inisol 1,4,5-triphosphate
<b>iPAH</b>	idiopathic pulmonary arterial hypertension
<b>ISH</b>	isolated systolic hypertension
<b>JVP</b>	jugular venous pressure
<b>LA</b>	left atrium

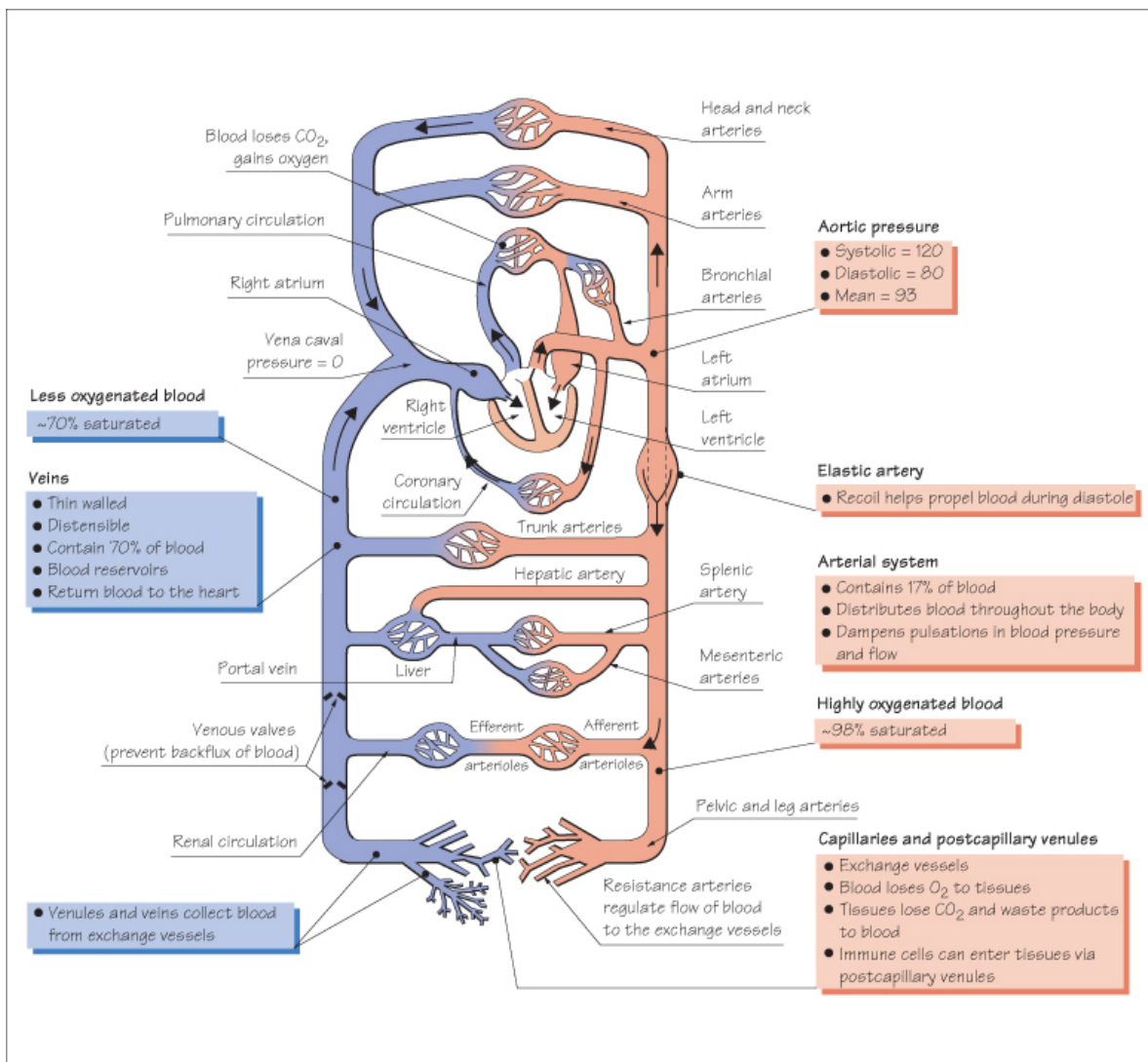
<b>LDL</b>	low-density lipoprotein
<b>LITA</b>	left internal thoracic artery
<b>LMWH</b>	low molecular weight heparin
<b>L-NAME</b>	L-nitro arginine methyl ester
<b>LPL</b>	lipoprotein lipase
<b>LQT</b>	long QT
<b>LV</b>	left ventricle/left ventricular
<b>LVH</b>	left ventricular hypertrophy
<b>MABP</b>	mean arterial blood pressure
<b>MCH</b>	mean cell haemoglobin
<b>MCHC</b>	mean cell haemoglobin concentration
<b>MCV</b>	mean cell volume
<b>MI</b>	myocardial infarction
<b>MLCK</b>	myosin light-chain kinase
<b>mPAP</b>	mean pressure in the pulmonary artery
<b>MR</b>	mitral regurgitation
<b>MRI</b>	magnetic resonance imaging
<b>MS</b>	mitral stenosis
<b>MW</b>	molecular weight
<b>NCX</b>	$\text{Na}^+ - \text{Ca}^{2+}$ exchanger
<b>NK</b>	natural killer
<b>NO</b>	nitric oxide
<b>NOS</b>	nitric oxide synthase
<b>nNOS</b>	neuronal nitric oxide synthase
<b>NSAID</b>	non-steroidal anti-inflammatory drug
<b>NSCC</b>	non-selective cation channel
<b>NSTEMI</b>	non-ST segment elevation myocardial infarction
<b>NTS</b>	nucleus tractus solitarius
<b>NYHA</b>	New York Heart Association
<b>PA</b>	postero-anterior
<b>PA</b>	pulmonary artery
<b>PAH</b>	pulmonary arterial hypertension
<b>PAI-1</b>	plasminogen activator inhibitor-1
<b>PCI</b>	percutaneous coronary intervention
<b>PCV</b>	packed cell volume
<b>PD</b>	potential difference

<b>PDA</b>	patent ductus arteriosus
<b>PDE</b>	phosphodiesterase
<b>PE</b>	pulmonary embolism
<b>PGE<sub>2</sub></b>	prostaglandin E <sub>2</sub>
<b>PGI<sub>2</sub></b>	prostacyclin
<b>PH</b>	pulmonary hypertension
<b>PI3K</b>	phosphatidylinositol 3-kinase
<b>PKA</b>	protein kinase A
<b>PKC</b>	protein kinase C
<b>PKG</b>	cyclic GMP-dependent protein kinase
<b>PLD</b>	phospholipid
<b>PMCA</b>	plasma membrane Ca <sup>2+</sup> -ATPase
<b>PMN</b>	polymorphonuclear leucocyte
<b>PND</b>	paroxysmal nocturnal dyspnoea
<b>PPAR</b>	proliferator-activated receptor
<b>PRU</b>	peripheral resistance unit
<b>PT</b>	prothrombin time
<b>PTCA</b>	percutaneous transcoronary angioplasty
<b>PVC</b>	premature ventricular contraction
<b>PVR</b>	pulmonary vascular resistance
<b>RAA</b>	renin-angiotensin-aldosterone
<b>RCA</b>	radiofrequency catheter ablation
<b>RCC</b>	red cell count
<b>RGC</b>	receptor-gated channel
<b>RMP</b>	resting membrane potential
<b>RV</b>	right ventricle/right ventricular
<b>RVLM</b>	rostral ventrolateral medulla
<b>RVOT</b>	right ventricular outflow tract tachycardia
<b>RyR</b>	ryanodine receptor
<b>SAN</b>	sinoatrial node
<b>SERCA</b>	smooth endoplasmic reticulum Ca <sup>2+</sup> -ATPase
<b>SHO</b>	senior house officer
<b>SK</b>	streptokinase
<b>SMTc</b>	S-methyl-L-thiocitrulline
<b>SOC</b>	

	store-operated $\text{Ca}^{2+}$ channel
<b>SPECT</b>	single photon emission computed tomography
<b>SR</b>	sarcoplasmic reticulum
<b>STEMI</b>	ST elevation myocardial infarction
<b>SV</b>	stroke volume
<b>SVR</b>	systemic vascular resistance
<b>SVT</b>	supraventricular tachycardia
<b>TAFI</b>	thrombin activated fibrinolysis inhibitor
<b>TAVI</b>	transcatheter aortic valve implantation
<b>TB</b>	tuberculosis
<b>TEE</b>	transthoracic echocardiogram
<b>TF</b>	tissue factor thromboplastin
<b>TFPI</b>	tissue factor pathway inhibitor
<b>TGF</b>	transforming growth factor
<b>TOE</b>	transoesophageal echocardiography/echocardiogram
<b>tPA</b>	tissue plasminogen activator
<b>TPR</b>	total peripheral resistance
<b>TRP</b>	transient receptor potential
<b>TXA<sub>2</sub></b>	thromboxane A <sub>2</sub>
<b>UA</b>	unstable angina
<b>uPA</b>	urokinase
<b>VF</b>	ventricular fibrillation
<b>VGC</b>	voltage-gated channel
<b>VLDL</b>	very low density lipoprotein
<b>VSD</b>	ventricular septal defect
<b>VSM</b>	vascular smooth muscle
<b>VT</b>	ventricular tachycardia
<b>VTE</b>	venous thromboembolism
<b>vWF</b>	von Willebrand factor
<b>WBCC</b>	white blood cell count
<b>WPW</b>	Wolff-Parkinson-White

# 1

## Overview of the Cardiovascular System



The cardiovascular system is composed of the heart, blood vessels and blood. In simple terms, its main functions are:



- 1** distribution of O<sub>2</sub> and nutrients (e.g. glucose, amino acids) to all body tissues
- 2** transportation of CO<sub>2</sub> and metabolic waste products (e.g. urea) from the tissues to the lungs and excretory organs
- 3** distribution of water, electrolytes and hormones throughout the body
- 4** contributing to the infrastructure of the immune system
- 5** thermoregulation.

**Blood** is composed of **plasma**, an aqueous solution containing electrolytes, proteins and other molecules, in which **cells** are suspended. The cells comprise 40-45% of blood volume and are mainly **erythrocytes**, but also **white blood cells** and **platelets**. Blood volume is about 5.5 L in an 'average' 70-kg man.

Figure 1 illustrates the 'plumbing' of the cardiovascular system.

Blood is driven through the cardiovascular system by the **heart**, a muscular pump divided into left and right sides. Each side contains two chambers, an **atrium** and a **ventricle**, composed mainly of cardiac muscle cells. The thin-walled atria serve to fill or 'prime' the thick-walled ventricles, which when full constrict forcefully, creating a pressure head that drives the blood out into the body. Blood enters and leaves each chamber of the heart through separate one-way valves, which open and close reciprocally (i.e. one closes before the other opens) to ensure that flow is unidirectional.

Consider the flow of blood, starting with its exit from the left ventricle.

When the ventricles contract, the left ventricular internal pressure rises from 0 to 120 mmHg (atmospheric pressure = 0). As the pressure rises, the aortic valve opens

and blood is expelled into the **aorta**, the first and largest artery of the **systemic circulation**. This period of ventricular contraction is termed **systole**. The maximal pressure during systole is called the **systolic pressure**, and it serves both to drive blood through the aorta and to distend the aorta, which is quite elastic. The aortic valve then closes, and the left ventricle relaxes so that it can be refilled with blood from the left atrium via the mitral valve. The period of relaxation is called **diastole**. During diastole aortic blood flow and pressure diminish but do not fall to zero, because *elastic recoil* of the aorta continues to exert a **diastolic pressure** on the blood, which gradually falls to a minimum level of about 80 mmHg. The difference between systolic and diastolic pressures is termed the **pulse pressure**. **Mean arterial blood pressure** (MABP) is pressure averaged over the entire cardiac cycle. Because the heart spends approximately 60% of the cardiac cycle in diastole, the MABP is approximately equal to the diastolic pressure + one-third of the pulse pressure, rather than to the arithmetic average of the systolic and diastolic pressures.

The blood flows from the aorta into the **major arteries**, each of which supplies blood to an organ or body region. These arteries divide and subdivide into smaller **muscular arteries**, which eventually give rise to the **arterioles** - arteries with diameters of  $<100\ \mu\text{m}$ . Blood enters the arterioles at a mean pressure of about 60–70 mmHg.

The walls of the arteries and arterioles have circumferentially arranged layers of **smooth muscle cells**. The lumen of the entire vascular system is lined by a monolayer of **endothelial cells**. These cells secrete vasoactive substances and serve as a barrier, restricting and controlling the movement of fluid, molecules and cells into and out of the vasculature.