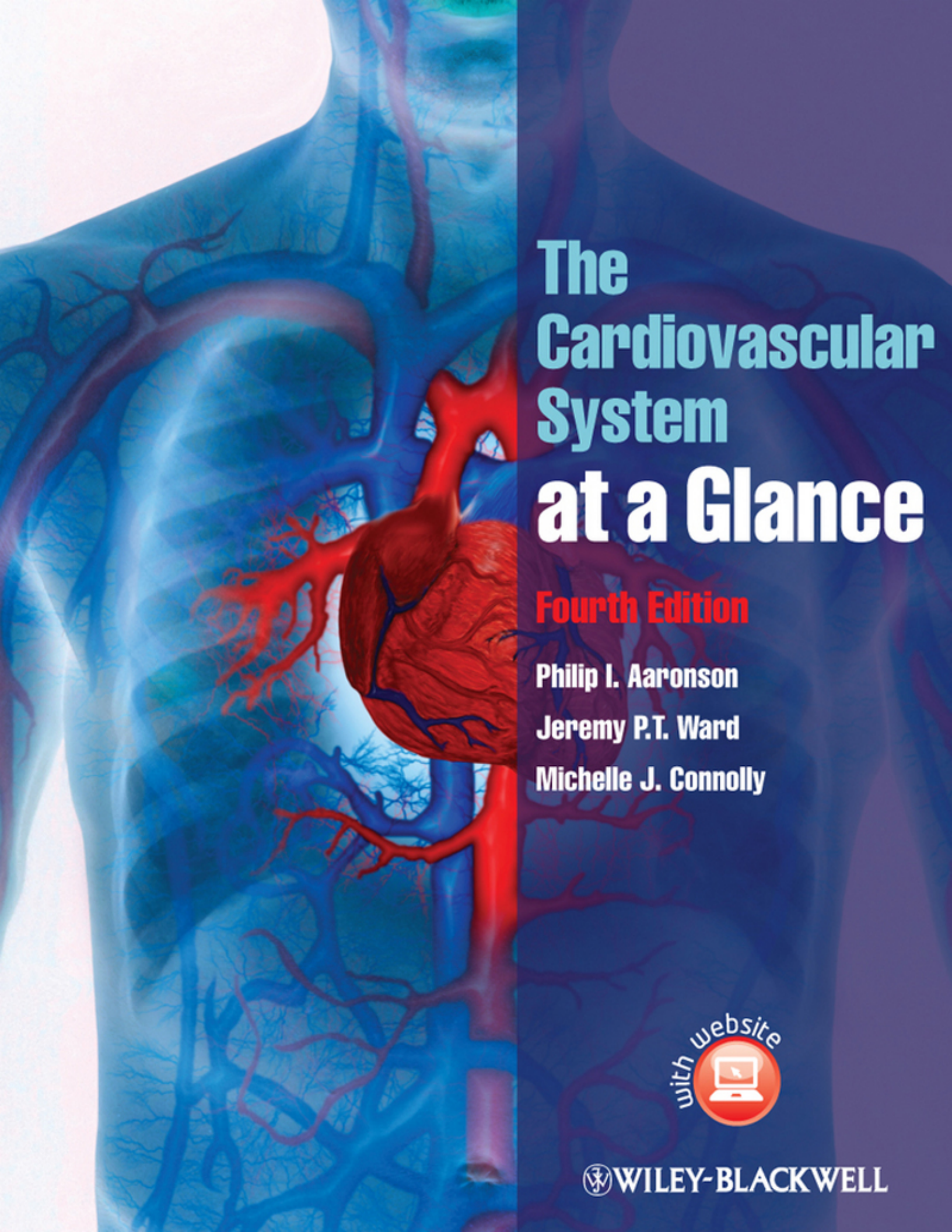

The Cardiovascular System at a Glance

Fourth Edition

Philip I. Aaronson
Jeremy P.T. Ward
Michelle J. Connolly

with website

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Table of Contents

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The Cardiovascular System at a Glance

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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.

Philip I. Aaronson
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

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

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

ECG	electrocardiogram/electrocardiograph (EKG)
ECM	extracellular matrix
EDHF	endothelium-derived hyperpolarizing factor
EDP	end-diastolic pressure
EDRF	endothelium-derived relaxing factor
EDTA	ethylenediaminetetraacetic acid
EDV	end-diastolic volume
EET	epoxyeicosatrienoic acid
EnaC	epithelial sodium channel
eNOS	endothelial NOS
ERP	effective refractory period
ESR	erythrocyte sedimentation rate
FDP	fibrin degradation product
GP	glycoprotein
GPI	glycoprotein inhibitor
GTN	glyceryl trinitrate
Hb	haemoglobin
HCM	hypertrophic cardiomyopathy
HDL	high-density lipoprotein
HEET	hydroxyeicosatetraenoic acid
HMG-CoA	hydroxy-methylglutanyl coenzyme A
hPAH	heritable pulmonary arterial hypertension
HPV	hypoxic pulmonary vasoconstriction
HR	heart rate
ICD	implantable cardioverter defibrillator
IDL	intermediate-density lipoprotein
Ig	immunoglobulin
IML	intermediolateral
iNOS	inducible NOS
INR	international normalized ratio
IP_3	inisotol 1,4,5-triphosphate
iPAH	idiopathic pulmonary arterial hypertension
ISH	isolated systolic hypertension
JVP	jugular venous pressure
LA	left atrium

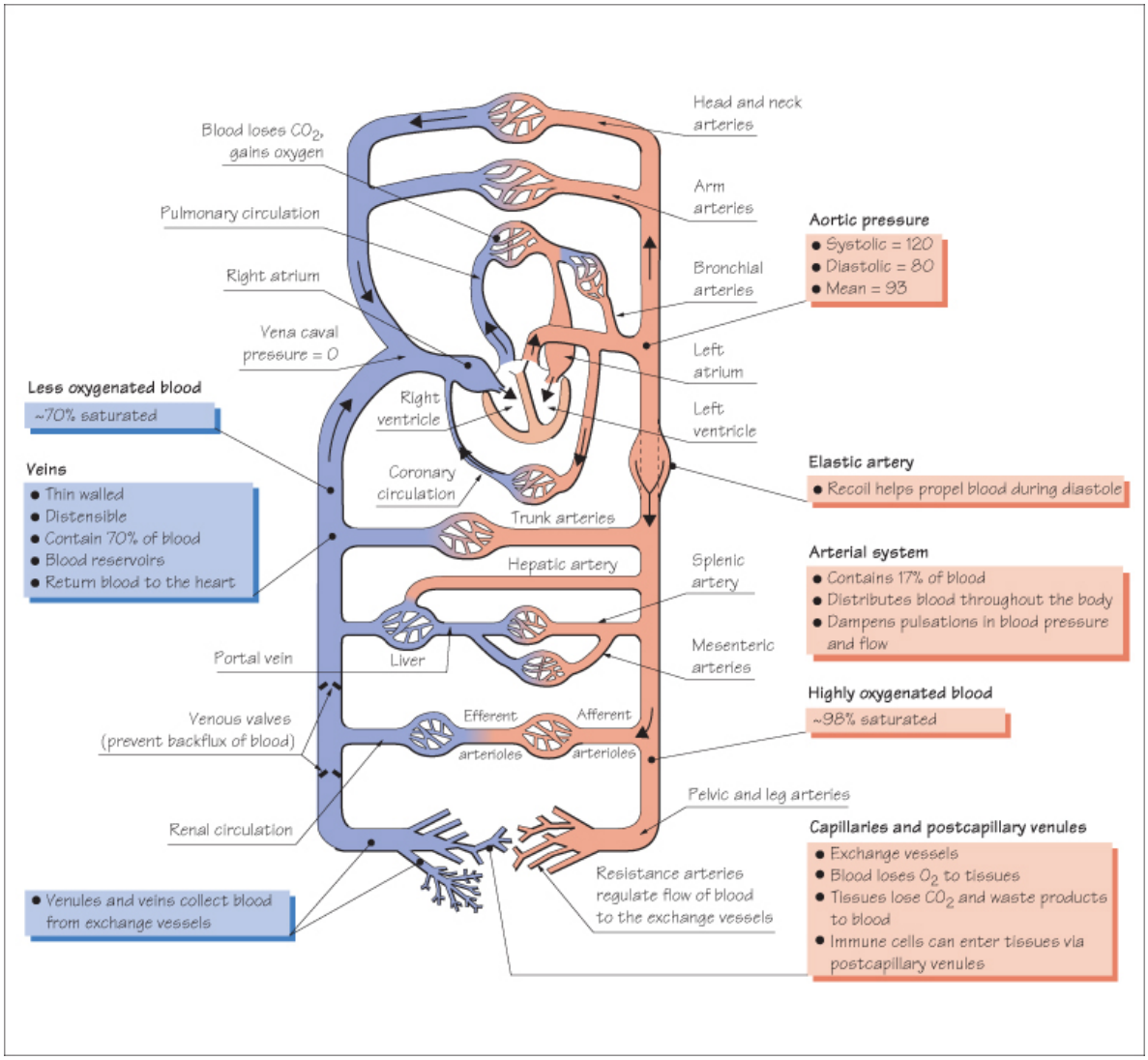
LDL	low-density lipoprotein
LITA	left internal thoracic artery
LMWH	low molecular weight heparin
L-NAME	L-nitro arginine methyl ester
LPL	lipoprotein lipase
LQT	long QT
LV	left ventricle/left ventricular
LVH	left ventricular hypertrophy
MABP	mean arterial blood pressure
MCH	mean cell haemoglobin
MCHC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

PDA patent ductus arteriosus
PDE phosphodiesterase
PE pulmonary embolism
PGE_2 prostaglandin E_2
PGI_2 prostacyclin
PH pulmonary hypertension
PI3K phosphatidylinositol 3-kinase
PKA protein kinase A
PKC protein kinase C
PKG cyclic GMP-dependent protein kinase
PLD phospholipid
PMCA plasma membrane Ca^{2+}-ATPase
PMN polymorphonuclear leucocyte
PND paroxysmal nocturnal dyspnoea
PPAR proliferator-activated receptor
PRU peripheral resistance unit
PT prothrombin time
PTCA percutaneous transcoronary angioplasty
PVC premature ventricular contraction
PVR pulmonary vascular resistance
RAA renin–angiotensin–aldosterone
RCA radiofrequency catheter ablation
RCC red cell count
RGC receptor-gated channel
RMP resting membrane potential
RV right ventricle/right ventricular
RVLM rostral ventrolateral medulla
RVOT right ventricular outflow tract tachycardia
RyR ryanodine receptor
SAN sinoatrial node
SERCA smooth endoplasmic reticulum Ca^{2+}-ATPase
SHO senior house officer
SK streptokinase
SMTC S-methyl-L-thiocitrulline
SOC

	store-operated Ca^{2+} channel
SPECT	single photon emission computed tomography
SR	sarcoplasmic reticulum
STEMI	ST elevation myocardial infarction
SV	stroke volume
SVR	systemic vascular resistance
SVT	supraventricular tachycardia
TAFI	thrombin activated fibrinolysis inhibitor
TAVI	transcatheter aortic valve implantation
TB	tuberculosis
TEE	transthoracic echocardiogram
TF	tissue factor thromboplastin
TFPI	tissue factor pathway inhibitor
TGF	transforming growth factor
TOE	transoesophageal echocardiography/echocardiogram
tPA	tissue plasminogen activator
TPR	total peripheral resistance
TRP	transient receptor potential
TXA_2	thromboxane A_2
UA	unstable angina
uPA	urokinase
VF	ventricular fibrillation
VGC	voltage-gated channel
VLDL	very low density lipoprotein
VSD	ventricular septal defect
VSM	vascular smooth muscle
VT	ventricular tachycardia
VTE	venous thromboembolism
vWF	von Willebrand factor
WBCC	white blood cell count
WPW	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_2 and nutrients (e.g. glucose, amino acids) to all body tissues

2 transportation of CO_2 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 μm. 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.