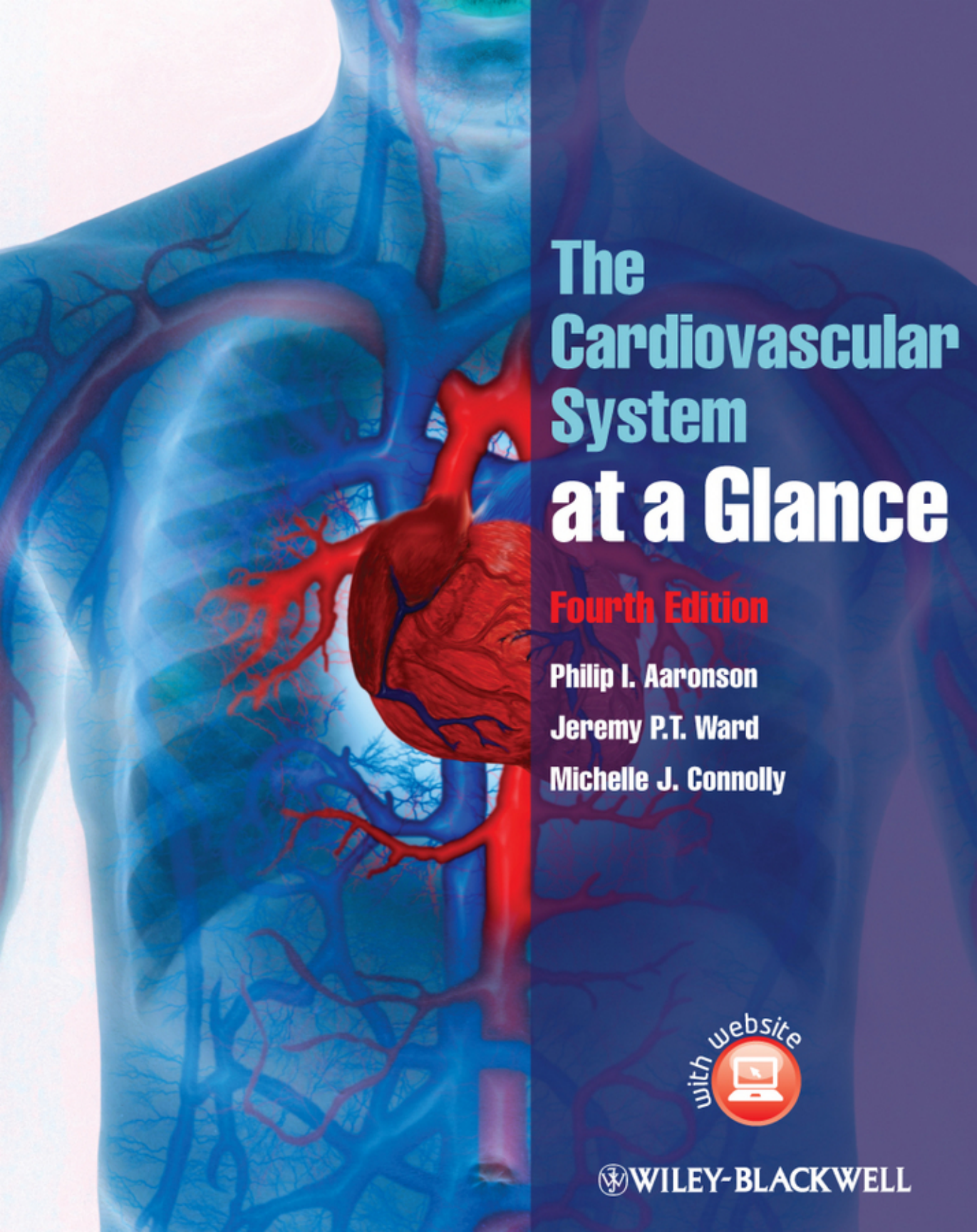

The Cardiovascular System at a Glance

Fourth Edition

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

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The Cardiovascular System at a Glance

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The Cardiovascular System at a Glance

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Fourth Edition

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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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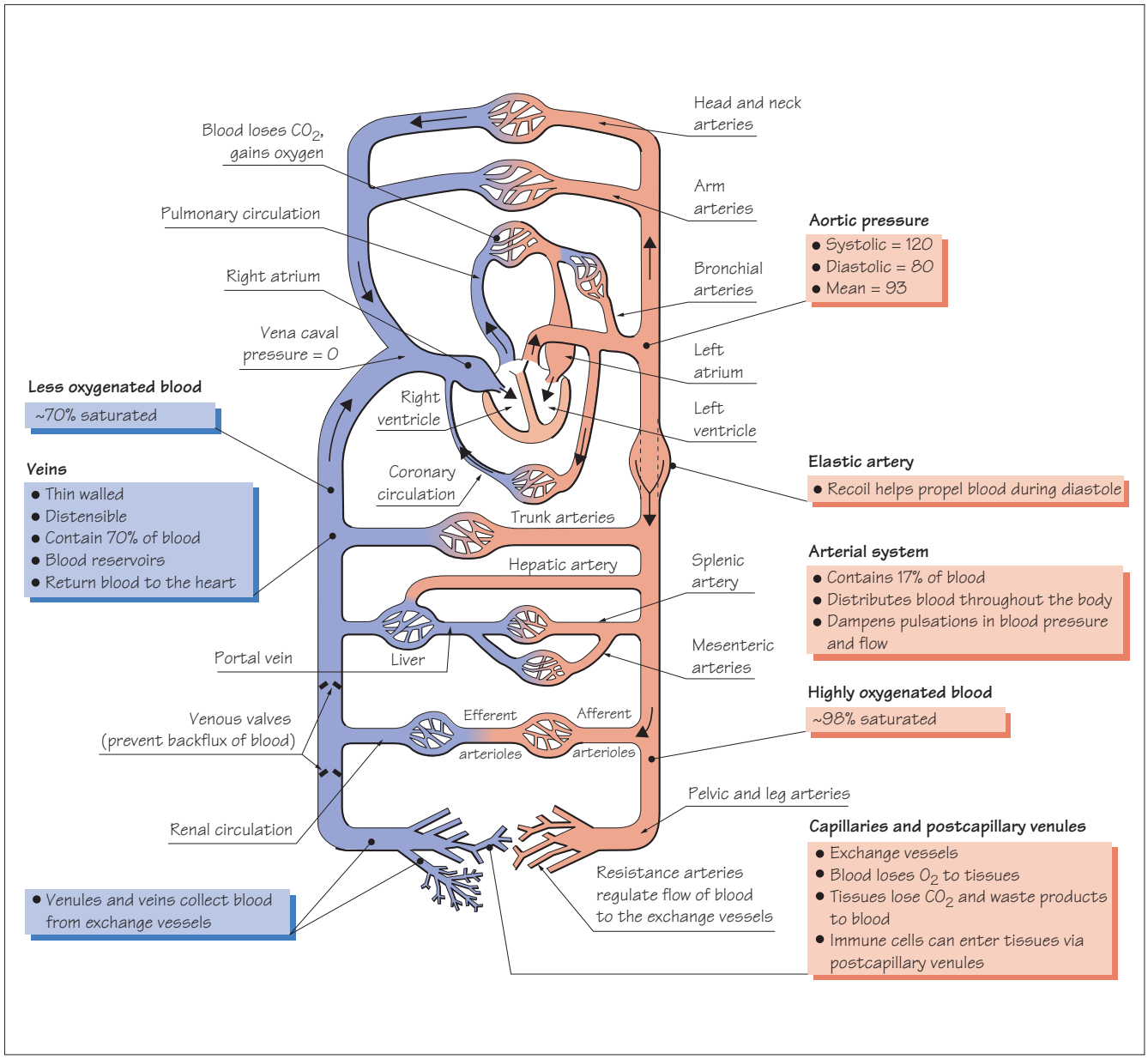
We are grateful to Karen Moore for her assistance in keeping track of our progress, putting up so gracefully with our missed deadlines, and generally making sure that this book and its companion website not only became a reality, but did so on schedule. Finally, as always, we thank our readers, particularly 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'

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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.

The arterioles lead to the smallest vessels, the **capillaries**, which form a dense network within all body tissues. The capillary wall is a layer of overlapping endothelial cells, with no smooth muscle cells. The pressure in the capillaries ranges from about 25 mmHg on the arterial side to 15 mmHg at the venous end. The capillaries converge into small **venules**, which also have thin walls of mainly endothelial cells. The venules merge into larger venules, with an increasing content of smooth muscle cells as they widen. These then converge to become **veins**, which progressively join to give rise to the **superior** and **inferior venae cavae**, through which blood returns to the right side of the heart. Veins have a larger diameter than arteries, and thus offer relatively little resistance to flow. The small pressure gradient between venules (15 mmHg) and the venae cavae (0 mmHg) is therefore sufficient to drive blood back to the heart.

Blood from the venae cavae enters the **right atrium**, and then the **right ventricle** through the **tricuspid valve**. Contraction of the right ventricle, simultaneous with that of the left ventricle, forces blood through the pulmonary valve into the pulmonary artery, which progressively subdivides to form the arteries, arterioles and capillaries of the **pulmonary circulation**. The pulmonary circulation is shorter and has a much lower pressure than the systemic circulation, with systolic and diastolic pressures of about 25 and 10 mmHg, respectively. The pulmonary capillary network within the lungs surrounds the alveoli of the lungs, allowing exchange of CO_2 for O_2. Oxygenated blood enters pulmonary venules and veins, and then the **left atrium**, which pumps it into the left ventricle for the next systemic cycle.

The output of the right ventricle is slightly lower than that of the left ventricle. This is because 1–2% of the systemic blood flow never reaches the right atrium, but is shunted to the left side of the heart via the bronchial circulation (Figure 1) and a small fraction of coronary blood flow drains into the thebesian veins (see Chapter 2).

Blood vessel functions

Each vessel type has important functions in addition to being a conduit for blood.

The branching system of elastic and muscular arteries progressively reduces the pulsations in blood pressure and flow imposed by the intermittent ventricular contractions.

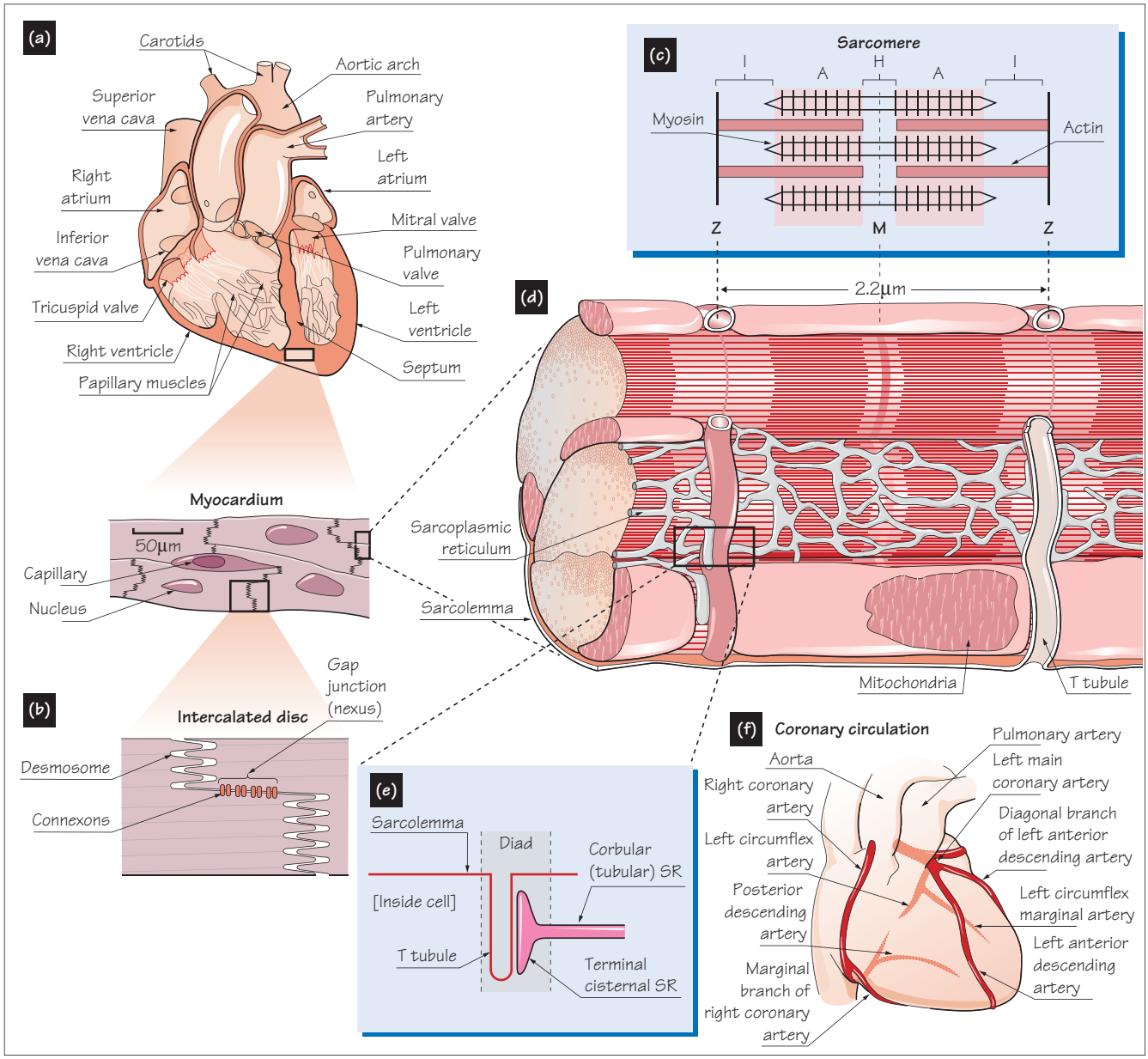
The smallest arteries and arterioles have a crucial role in regulating the amount of blood flowing to the tissues by dilating or constricting. This function is regulated by the sympathetic nervous system, and factors generated locally in tissues. These vessels are referred to as **resistance arteries**, because their constriction resists the flow of blood.

Capillaries and small venules are the **exchange vessels**. Through their walls, gases, fluids and molecules are transferred between blood and tissues. White blood cells can also pass through the venule walls to fight infection in the tissues.

Venules can constrict to offer resistance to the blood flow, and the ratio of arteriolar and venular resistance exerts an important influence on the movement of fluid between capillaries and tissues, thereby affecting blood volume.

The veins are thin walled and very *distensible*, and therefore contain about 70% of all blood in the cardiovascular system. The arteries contain just 17% of total blood volume. Veins and venules thus serve as volume reservoirs, which can shift blood from the peripheral circulation into the heart and arteries by constricting. In doing so, they can help to increase the **cardiac output** (volume of blood pumped by the heart per unit time), and they are also able to maintain the blood pressure and tissue perfusion in essential organs if **haemorrhage** (blood loss) occurs.

2 Gross anatomy and histology of the heart



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