

Encyclopedia of Heart Diseases

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With 255 Figures and 70 Tables

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To my wife Brigid who made this work possible

And to our children

Susan

Christine

Yasmin

Jacqueline

Stephen

Natasha

Acknowledgments

People who need people

The vast amount of information provided to readers is indicative of the efforts and perseverance of the numerous investigators whose published works I have had the pleasure of quoting. These talented *women and men* of medicine deserve my respect, my thanks, and my congratulations. I feel certain, however, that the names of many researchers have been omitted because of my oversight and because references provide only three names.

Sandra Fabiani: Executive Editor, my Publisher at Springer, had the foresight to accept my proposal; without her remarkable vision, this second edition would not have emerged.

I must express my thanks to Susanne Friedrichsen, Associate Editor, and her team that includes:

- Ulrike Eggert-Neben, Editorial Assistant
- Chandramohan Sivasubramanian, Project Manager who faced the task of production of the book without disappointing me with their patience for accepting my numerous additional updates.

The printing style is what I requested – a text that is noncompressed, user friendly, and with well-positioned illustrations. Few publishers are able to follow the whims of authors.

Last, I must thank Doctors Scott Solomon and Bernard Bulwer for allowing me to use animated echocardiographic images fetched from their book *Essential Echocardiography*.

There is little doubt, however, that without the love and commitment of my wife Brigid, this daunting task of the production of a single-authored, 96-chapter encyclopedia would not have been possible.



Preface

Cardiovascular disease currently is responsible for more than 14 million deaths worldwide annually and is estimated that this will increase to more than 25 million deaths in the year 2025 in a population of 7.9 billion people. This widespread disease causes more deaths than all forms of cancer, diabetes, infections, and lung diseases. This epidemic can only be curbed by relevant and sound research. Such research, however, requires acquisition of accurate core knowledge. The budding researcher needs to know what is truly proven and what needs to be proven.

Clinicians require online medical updates brought rapidly to their computers so as to render more efficient care for their patients.

- This encyclopedic work is directed at all physicians who render care to cardiovascular patients and to all who wish to pursue a research career in medicine, pharmacology, biomedical engineering, and technologic innovations. Hopefully, practicing clinicians would glean crucial and up-to-date information that would provide ameliorating benefits for their patients. At the end of a patient–doctor consultation, it is the prescription handed to the patient that provides a cure or salutary effect. Thus, the text gives considerable amount of information on cardiovascular therapeutics.
- Both career researchers and those who wish to devote only a few years in research will find the information provided invaluable. Postgraduates in science and technology, including MDs and PhDs, who wish to pursue research in the medical sciences must have a reference source that provides core knowledge in medicine, particularly, pathogenesis, pathophysiology, clinical diagnostic features, diagnostic techniques, and management strategies. The text provides this information.
- In addition, our senior college youth worldwide are clamoring for new knowledge that is not provided by tutors who prefer students to research topics. Much is provided by the internet but inaccuracy abounds. Some material in the text is at times simplified to reach the college audience.
- The text often describes historical events that led up to certain hallmark discoveries; this is done to indicate to those interested in research that simple thoughts and perseverance bring fruits from research. It is my hope that this historical and relevant cardiologic information will provide motivation and awakening of new interests in the solving of the pathogenesis, pathophysiology, diagnosis, and management strategies of a variety of heart diseases.
- Often, major discoveries are made by those who pursue only a few years in research, and innovations may be made by simple thought processes. A prime example is the one revealed by Reverend Hales, the father of hemodynamic medicine. During his studies in theology at Cambridge, he was fortunate to do mathematics and science and had conversations with a medical student. In 1733, after many years in his ministry, at Teddington outside London, he found the time for the study of circulation. Figure 1 in the entry ► [Blood Pressure](#) shows Hales observing the blood pressure in a horse, and he is credited to be the first to demonstrate the measurement of blood pressure.
- The vascular surgeon Korotokoff, in Russia in 1900, recognizing that a constricted artery makes no sound, used a stethoscope to observe the sounds made by the blood flowing through the artery in the arm constricted by an arm band; he heard sounds as the band was released. The first sounds were taken as the systolic blood pressure and the sounds are called Korotkoff sounds; the technique is used to this day without change. Korotokoff’s innovative discovery required only his thought of sound; he was not a researcher. Surgeons do not normally use stethoscopes but vascular surgeons do so, because they listen over expanded arteries, aneurysms that emit a loud bruit, a sound made as the blood strikes the expanded wall of the artery.
- Many of the technologic advances in medicine have been provided for us by the collaboration of engineers, physicists, biologists, and medical doctors. Einthoven would not have produced the electrocardiogram in 1901, if Adler had not provided the wireless telegraph; also, the string galvanometer, a nonmedical device, was then available to Einthoven.
- The advent of ultrasonography was an innovation prompted by the Titanic disaster and the underwater search for submarines in 1939. At the end of the war, physicists and medical doctors collaborated to provide the ultrasound for neurologic investigations. Echocardiography stemmed from an engineer who worked in collaboration with a medical student and a physician. In 1964, Dr. Harvey Feigenbaum saw the unsophisticated machine at the American college of

cardiology scientific session. He went back to his lab and borrowed an ultrasound machine from the neurosurgical division and used this to show that pericardial effusions around the heart could be observed by ultrasonic technique and presented his hallmark paper (Feigenbaum 2008).

His research work was not overwhelming and did not require much scientific thought or expertise. He was not a major research scientist. Many of the advances in echocardiography during 1965 to 1990 can be attributed to his work and to the sophistication by the engineers.

- Bernard Lown is credited in the Western world with initiating the modern era of cardioversion (Cakulev et al. 2009). Lown recalled the following:
 - ▶ Never having seen an AC defibrillator, I hadn't the remotest idea how to use one. A host of questions needed prompt answers: Was the shock painful? Was the anesthesia required? Was there an appropriate voltage setting to reverse ventricular tachycardia? If the shock failed, how many additional ones could be delivered?(Lown 1996)

He “fortunately, and quite accidentally, met a brilliant young electrical engineer, Baruch Berkowitz,” who had been developing a DC defibrillator while working for the American Optical Corporation. Berkowitz in 1961 had the instrument tested in animals by Bernard Lown (Lown 1996).

Medical science has made huge progress in the past few decades but far more remains unresolved. A prime example is the knowledge that is available on the development of atheroma and atherothrombosis, a disease process responsible for heart attacks, angina, sudden deaths, stroke, intermittent claudication, and gangrene of the leg. The word atheroma is derived from the Greek word “athere,” meaning porridge or gruel. Ancient Greek physicians removed the plaques of atheroma that obstructed arteries, and cutting the plaque of atheroma revealed a gelatinous porridge-like material. At least, we do know that the porridge-like material which exudes from a ruptured atheromatous plaque is highly thrombogenic and promotes the clotting of circulating blood, and thus the arterial occlusion which results in myocardial infarction (heart attack) or cerebral infarctions (strokes).

Atheroma is the basis for heart attacks and stroke and is mainly responsible for the epidemic described above. After more than 60 years of research, we do not know how to effectively prevent the atheroma formation and its progression to vessel occlusion. Our new diagnostic armamentarium includes CT calcium scoring and CT coronary angiograms, both of which generates unjustifiable radiation hazards and give only clues to the presence of vulnerable atheromatous plaques. MRI is of limited value. The information gleaned from the results of these tests most often do not significantly alter the therapy for the millions affected worldwide by the epidemic of atheromatous cardiovascular disease.

Developments of technologic instruments that may provide noninvasive detection of atheromatous obstruction in coronary arteries that presently can only be observed with certainty by an invasive coronary angiography are urgently required. CT coronary angiography provides considerable information but is not a substitute for an invasive coronary angiography which gives the crucial information required for a percutaneous coronary intervention or a bypass surgery.

The information provided in this reference work is mainly factual and does not discuss controversies. But, two entries of the 96, of necessity, discuss two recent and important controversies in cardiovascular medicine.

1. Worldwide, there are more than one billion hypertensive individuals who require drug treatment. Sadly, after more than 70 years of research, there are only four drugs available: diuretics, beta blockers, calcium antagonists, and ACE inhibitors (angiotensin receptor blockers are similar agents). Other agents: methyldopa is used mainly for hypertension in pregnancy and alpha blockers cause heart failure and hence its use is restricted. This situation can only be corrected if pharmaceutical firms and experts in the field of hypertension recognize that only four drugs are available.

More than 60% of hypertensive patients require two or three drugs to attain blood pressure control.

- Recently, peer-reviewed journals have provided editorials by notable physicians who state that the beta blockers should not be prescribed for primary hypertension because of their ineffectiveness and they may cause diabetes. An entry entitled ▶ [Beta Blockers Hypertension Controversy](#) addresses this topic that is important for clinicians worldwide.

2. Increase in the incidence of diabetes is a concern: Many investigators have reported recently in peer-reviewed journals that diuretics and beta blockers cause diabetes mellitus and their use should be restricted. This information would greatly decrease the prescribing of two of the only four antihypertensive agents available. These two agents are

inexpensive and enjoyed beneficial use for more than 40 years. An entry, ► [Diabetes Caused by Diuretics and Beta Blockers](#) gives directions and advice that should be helpful to physicians globally.

- One of the longest entries in this book, ► [Clinical Trials](#), gives the results of numerous hallmark randomized clinical trials. The vast amount of information provided to readers is indicative of the efforts and perseverance of the numerous investigators whose published works I have had the pleasure of quoting. *These talented women and men of medicine deserve my respect, my thanks, and congratulations.*
- More than 80% of the material contained in the first edition has been replaced by new information and written at a higher level to reach postgraduates in medicine, internists, general practitioners, pharmacologists, biologists, and researchers. The entire work has been revised and thoroughly updated. In addition, there are 13 new entries.

The text gives numerous illustrations to provide the reader with relevant insights and to render the material more user friendly.

- This second edition in its electronic format should be offered online at hospital libraries and university and general libraries, so that accurate core knowledge in cardiovascular medicine is available, for use by, students, clinicians, researchers, including engineers, and all who wish to quell the worldwide epidemic of cardiovascular disease. Online updates will be provided in regular terms.

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M. Gabriel Khan



Foreword

With the enormous burden of heart disease in the world, most physicians and healthcare professionals spend large portions of their time managing cardiovascular disease and risk factors. Recent data have seen that this is not just in the developed world, but also globally in all nations as risk factors such as smoking and obesity spread.

As such, clinicians need to be up to date on all aspects of cardiovascular disease – both the pathophysiology of disease, but also the current recommended treatments.

So, what would we want from an encyclopedia on heart disease? Ideally, a book would be comprehensive, yet concise, and be practically oriented, and explain pathophysiology and treatment. In addition, it should be accessible online so that it can be accessed at the bedside or anywhere.

Dr. Khan has written exactly such a book. *Encyclopedia of Heart Diseases* is comprehensive, yet concise, and very practically oriented. Importantly, it takes a step-by-step approach, walking the reader through a thorough pathophysiology of conditions, their evaluation and treatment. For therapies, he provides the mechanism of the drug, its doses, side effects and clinical efficacy.

A key component of the book is that it was designed to be an online resource. As such, the information is in short readable formats – and hyperlinked to relevant other sections. It becomes a terrific online resource with all the information you need!

Dr. Khan is to be congratulated on an outstanding text/resource that will help readers/users improve their care of heart disease.

Christopher P. Cannon, MD
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About the Author

Dr. M Gabriel Khan is a cardiologist at the Ottawa Hospital and an Associate Professor of Medicine at the University of Ottawa. Dr. Khan graduated MB, BCh, with First Class Honors at The Queen's University of Belfast. He is a Fellow of the American College of Cardiology, the American College of Physicians, and the Royal College of Physicians of London and Canada.

He is the author of:

Cardiac Drug Therapy, seventh edition, 2007, Humana Press, New York

On Call Cardiology, third edition, 2006, W.B. Saunders/Elsevier, Philadelphia

Rapid ECG Interpretation, third edition, 2008, Humana Press, Springer New York

Cardiac and Pulmonary Management, 1993, Lea & Febiger, Philadelphia

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Heart Attacks, Hypertension and Heart Drugs, second edition, 1990, Bantam/Seal, Toronto

Heart Trouble Encyclopedia, 1996, Stoddart, Toronto

Heart Disease Diagnosis and Therapy, a Practical Approach, first edition, Williams & Wilkins, 1996; second edition, 2005, Humana Press, New Jersey

Encyclopedia of Heart Diseases, first edition, 2005, Academic Press/Elsevier, San Diego

His books are read worldwide, having acquired foreign translations: Chinese, French, Farsi, German, Greek, Italian, Japanese, Polish, Portuguese, Russian, Spanish, and Turkish.

Here is an excerpt from the foreword, written by a renowned cardiologist and author, Dr. Henry J. L. Marriott for the book, *Heart Disease Diagnosis and Therapy*:

► "Whenever I read Khan, I am affected as the rustics were by Oliver Goldsmith's parson:

And still they gaz'd, and still the wonder grew

That one small head could carry all he knew.

Khan's knowledge is truly encyclopedic and, for his fortunate readers, he translates it into easily read prose."

And for the book *Cardiac Drug Therapy*, fourth edition, a cardiologist reviewer states, "By far the best handbook on cardiovascular therapeutics I have ever had the pleasure of reading. The information given in each chapter is up-to-date, accurate, clearly written, eminently readable and well referenced."

And from *Clinical Cardiology*, a review of the fifth edition of *Cardiac Drug Therapy*, "This is an excellent book. It succeeds in a very practical way while presenting the major evidence in relation to its recommendations. From the trainee to the experienced consultant, all will find it useful. The author stamps his authority very clearly throughout the text by very clear assertions of his own recommendations even when these recommendations are at odds with those of official bodies. In such situations the 'official' recommendations are also stated but clearly are not preferred."



List of Abbreviations

%	Percent	CVS	Cardiovascular system
<	Less than	DBP	Diastolic Blood Pressure
>	Greater than; more than	DCM	Dilated cardiomyopathy
≤	Equal to or less than	dL (dL)	Deciliter
χ square	Chi-square test	DSE	Dobutamine Stress Echocardiography
ACC	American College of Cardiology	DVT	Deep venous thrombosis
ACE	Angiotensin-converting enzyme	EBCT	Cardiovascular Electron Beam Computerized Tomography
ACS	Acute coronary syndrome	ECG	Electrocardiogram, electrocardiographic
ACTH	Adreno-Cortico-Tropic Hormone	EE	Exercise Echocardiography
AED	Automated external defibrillator	EF	Ejection fraction
AF	Atrial fibrillation	EIA	Enzyme Immuno-Assay
AHA	American Heart Association	EMD	Electromechanical dissociation
ARB	Angiotensin Receptor Blockers	eNOS	Endothelial-type NO Synthase
ASD	Atrial septal defect	EP	Electrophysiologic
ASO	Amplatzer Septal Occluder	ESC	European Society of Cardiology
ATP	Adenosine Triphosphate	ESH	European Society of Hypertension
AV	Atrioventricular Node	FAST-PCI	Reduced-dose fibrinolytic acceleration of STEMI treatment followed by urgent percutaneous coronary intervention
AVM	Arteriovenous Malformations	FDA	Food and Drug Administration
AVNRT	A-V nodal reentrant tachycardia	g	Gram
BHAT	Beta Blocker Heart Attack Trial	GFR	Glomerular filtration rate
bid	Twice a day	GI	Gastrointestinal
BMI	Body-Mass-Index	GU	Genitourinary
BNP	B-type Natriuretic Peptide	HCM	Hypertrophic cardiomyopathy
BP	Blood pressure	HCTZ	Hydrochlorothiazide
CABG	Coronary bypass graft	HDL	High density lipoprotein cholesterol
CABS	Coronary artery bypass surgery	HF	Heart failure
CAD	Coronary artery disease	HFNEF	HF with Normal EF
CCTA	Coronary computed tomographic angiography	HFPEF	Heart failure preserved EF
CHD	Coronary heart disease	HIV	Human Immunodeficiency Virus
CHF	Congestive heart failure	HR	Hazard Ratio
CI	Confidence Interval	HR-2DTTE	High Resolution two-Dimensional Transthoracic Echocardiography
CK	Creatine kinase	hs CRP	High sensitive C-Reactive Protein
CK-MB	Creatine Kinase-MB	IABP	Intra-Aortic Balloon Pump
CMR	Cardiovascular magnetic resonance	ICA	Invasive coronary angiography
CO	Carbon Monoxide	ICD	Implantable Cardioverter Defibrillator
COA	Coarctation of the Aorta	IE	Infective Endocarditis
COPD	Chronic obstructive pulmonary disease	IGI	Insulinogenic Index
CPK	Creatine phosphokinase	IHD	Ischemic heart disease
CPR	Cardiopulmonary resuscitation	IM	Intramuscular
CRT	Cardiac Resynchronization Therapy	iNOS	Induce Nitric Oxide Synthase
CRT-D	Cardiac Resynchronization Therapy plus defibrillator	INR	International normalized ratio
CS	Cardiogenic Shock	IR	Insulin Resistance
CT	Computed tomography; computerized tomographic		
CVD	Cardiovascular Disease		

ISA	Intrinsic Sympathomimetic Activity	PET	Positron Emission Tomography
ISDN	Iso-Sorbide Di-Nitrate	PLAX	Parasternal Long-Axis view
IV	Intravenously	PPH	Primary Pulmonary Hypertension
IVCD	Intraventricular conduction delay	PS	Pulmonary Stenosis
JVP	Jugular venous pressure	PVC	Premature Ventricular Contractions
Kg	Kilogram	PVD	Peripheral Vascular Disease
LAD	Left Anterior Descending Coronary Artery	RAAS	Renin Angiotensin Aldosterone System
LBBB	Left bundle branch block	RBBB	Right bundle branch block
LDL	Low density lipoprotein cholesterol	RCTs	Randomized clinical trials
LV	Left Ventricular	ROS	Reactive Oxygen Species
LVEF	Left Ventricular Ejection Fraction	RR	Relative risk
LVH	Left ventricular hypertrophy	RT3DE	Real-Time Three-Dimensional Imaging
MCE	Myocardial Contrast Echocardiography	RV	Right Ventricular
MI	Myocardial infarction	SA	Sinoatrial Node
Mmol/L	Millimoles per liter	SBP	Systolic Blood Pressure
MMP	Matrix Metalloproteinase	SDB	Sleep disordered breathing
MRC	Medical Research Council	STEMI	ST-Elevation Myocardial Infarction
MRI	Magnetic resonance imaging	SVT	Supraventricular tachycardia
mRNA	Messenger Ribonucleic acid	TDI	Tissue Doppler Imaging
NF	Nuclear Factor	TEE	Trans-Esophageal Echocardiography
NO	Nitric Oxide	TFR	Trans-Ferrin Receptor
NSAID	Nonsteroidal Anti-Inflammatory Drugs	TIA	Transient ischemic attack
NSTEMI	Non-ST-Elevation Myocardial Infarction	TOF	Tetralogy of Fallot
NYHA	New York Heart Association	tPA	Tissue Plasminogen Activator
OR	Odds ratio	UKPDS	UK Prospective Diabetes Study Group
OSA	Obstructive sleep apnea	VEGF	Vascular Endothelial Growth Factor
PA	Postero-Anterior	VF	Ventricular fibrillation
PAH	Pulmonary Arterial Hypertension	VPB	Ventricular premature beat
PAI-1	Type-1 Plasminogen Activator Inhibitor	VSD	Ventricular septal defect
PCI	Percutaneous coronary intervention	VT	Ventricular Tachycardia
PCWP	Pulmonary Capillary Wedge Pressure	WHO	World Health Organization
PDA	Patent Ductus Arteriosus	WPW	Wolff–Parkinson–White syndrome