



# Myocardial Metabolism in Heart Failure

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## Abstract

**Purpose of Review** Myocardial metabolism is intricately linked to cardiac function. Perturbations of cardiac energy metabolism result in an energy-starved heart and the development of contractile dysfunction. In this review, we discuss alterations in myocardial energy supply, transcriptional changes in response to different energy demands, and mitochondrial function in the development of heart failure.

**Recent Findings** Recent studies on substrate modulation through modifying energy substrate supply have shown cardio-protective properties. In addition, large cardiovascular outcome trials of anti-diabetic agents have demonstrated prognostic benefit, suggesting the importance of myocardial metabolism in cardiac function.

**Summary** Understanding molecular and transcriptional controls of cardiac metabolism promises new research avenues for metabolic treatment targets. Future studies assessing the impact of substrate modulation on cardiac energetic status and function will better inform development of metabolic therapies.

**Keywords** Myocardial metabolism · Heart failure · Substrate utilisation · Metabolic inflexibility

## Introduction

A salient feature of the heart is its metabolic flexibility [1], allowing it to efficiently adapt to varying ATP demands through utilisation of multiple energy substrates such as fatty acids, glucose, lactate, ketones, and amino acids. This is achieved through a complex network of interacting metabolic pathways involving each class of energy substrate, which in turn is capable of remodelling in chronic pathophysiological conditions [2]. As cardiac function is intricately linked to its metabolism, alterations in metabolic pathways can lead to morphological and functional changes. This is seen most clearly in heart failure, where metabolic inflexibility and energetic deficit are associated with maladaptive metabolic remodelling [3, 4].

This review aims to provide an overview of cardiac metabolism in heart failure at its three most important stages: [1] substrate utilisation, [2] ATP generation, and [3] ATP transport and stores. The role of mitochondrial function in the development of heart failure, the importance of transcriptional and post-translational modification in the regulation of cardiac metabolism, and an overview of how perturbations in this tightly regulated system can lead to the development of cardiac dysfunction are included.

## Cardiac Metabolism in the Normal Heart

### Step 1: Substrate Uptake and Metabolism

The first stage of cardiac metabolism is substrate delivery, uptake, and generation of acetyl-CoA to facilitate entry into the tricarboxylic acid (TCA) cycle [5, 6•]. Under basal conditions, the majority of acetyl-CoA formation is from long-chain fatty acyl-coenzyme A (60–90%) and pyruvate (10–40%, derived equally from glycolysis and lactate) [7, 8]. Alternative sources such as ketone bodies and amino acids form a minor source of ATP generation under normal physiological conditions.

The selection of energy substrate for ATP production depends on substrate availability, energy demands, and the

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# Myocardial Metabolism Recent Advances In Studies On Cardiac Structure And Metabolism

**International Study Group for  
Research in Cardiac Metabolism**



## **Myocardial Metabolism Recent Advances In Studies On Cardiac Structure And Metabolism:**

Recent Advances in Studies on Cardiac Structure and Metabolism International Society for Heart Research, 1978

*Advances in Myocardiology* Eugene I. Chazov, 2013-06-29 This volume of *Advances in Myocardiology* is derived from a part of the proceedings of the 10th Congress of the International Society for Heart Research which was held in Moscow on September 23-29, 1980. This book contains selected papers which have been arranged in two sections: Cardiac Hypertrophy, Adaptation and Pathophysiology, and Cardiac Hypoxia, Ischemia and Infarction. The first section on the pathophysiology of heart hypertrophy and failure contains 24 chapters that focus on the derangement of biochemical, physiological, and immunological processes during the development of heart disease due to a wide variety of pathogenic factors. Some of the recent developments in understanding the myocardial synthetic machinery in heart hypertrophy are also described in these papers, and we believe that the contents of this section will stimulate further research in the area of heart disease. The second section, which mainly deals with myocardial ischemia, contains 35 chapters providing the necessary background for the diagnosis of ischemic heart disease and some possible therapeutic approaches. It hardly needs to be emphasized that ischemic heart disease is a major cause of death in highly industrialized countries, but unfortunately the exact mechanism by which ischemic insult leads to the development of heart cell damage is far from understood. We are hopeful that the articles in this section will provide valuable information in this field and thus will help in improving the treatment of ischemic heart disease.

**Physiology and Pathophysiology of the Heart** Nicholas Sperelakis, 2013-06-29 could go on for several pages. Thus the book edited by Sperelakis emphasizes the fundamental functional aspects of cardiology. Within the last thirty years by Sperelakis is a potent reminder of the almost total rift between clinical and investigative cardiology. The fact that cardiology has two sites inextricably has widened because of the overwhelmingly developmentally related development of new clinical procedures, both diagnostic and therapeutic. The book deals with subjects in which Dr. Sperelakis and his colleagues have pioneered. Almost forgotten is the fact that Sperelakis has pioneered ultrastructure of heart muscle; we owe most of the clinical advances to theoretical electrophysiology, cardiac contractility, and ion exchange and experimental observations. I need not remind you that an extension of these subjects is the chapter on the work of Carrel who performed the dealing with fundamental topics of the coronary circulation. First experimental coronary bypass in 1902 or the culmination work of the brothers Curie in 1880, both physicists. This book is indeed a timely reminder of the man who discovered piezoelectricity, the keystone in the importance of the fundamental aspects of cardiology. Radiography of the works of Langley who introduced emphasis on clinical aspects of cardiology alone will deduce the receptors concept of Ahlquist in 1946 results in a sterile and unproductive future for a field who first differentiated between alpha and beta receptors that has made such stunning advances during the development of Fleckenstein, a physiologist who in the last thirty years has benefited millions of people.

*Heart Muscle: Ultrastructural Studies* Visvan Navaratnam, 1987-11-26

*Biochemistry and Pharmacology of Myocardial Hypertrophy, Hypoxia, and Infarction* International Study Group for

Research in Cardiac Metabolism,1976      **Cardiac Metabolism in Health and Disease** Salah Abdel-aleem,James E. Lowe,2012-12-06 This special issue of Molecular and Cellular Biochemistry contains original research papers as well as invited reviews focused in the field of cardiac metabolism and its regulation under normal and disease conditions These papers cover many areas under intensive and rapid development such as the regulation of fatty acid oxidation in the heart the role of cardiac glycogen during ischemia the role of CPT I isoenzymes the pathophysiology of diabetic cardiomyopathy cardiac protection through regulation of energy production the role of fatty acid binding protein under normal and pathological conditions and several other important topics in this area of research We hope that this special issue of Molecular and Cellular Biochemistry provides an up to date source of information for scientists and clinicians interested in the mechanism by which cardiac metabolism is regulated in health and disease and the mechanistic relationship between disturbances in cardiac metabolism and the genesis of cardiovascular diseases      **Catecholamines and Stress** Earl Usdin,Richard Kvetnanský,Irwin J. Kopin,2014-05-08 Catecholamines and Stress covers the proceedings of the International Symposium on Catecholamines and Stress held in Bratislava Czechoslovakia on July 27 30 1975 This book mainly focuses on catecholamines and stress presenting papers specifically discussing the brain neurohumoral regulation in stress and changes induced by stress A set of papers tackle the catecholamine synthesizing and degrading enzymes under stress Other papers are devoted to topics on catecholamine synthesis and degradation under stress release level and excretion of catecholamines in stress and catecholamines and stress in man This text will be invaluable to students and experts in physiology biology and related fields      Magnesium Deficiency in the Pathogenesis of Disease Mildred S. Seelig,2012-12-06 There is a large and rapidly growing body of literature on the importance of magnesium in biochemical and physiological processes There is also much evidence that magnesium deficiency alone and in combination with agents that interfere with its utilization is associated with functional and structural abnormalities of membranes cells organs and systems The manifestations of the changes caused by magnesium deficiency depend upon its extent and duration and on variable factors Among the conditions that increase the risk of magnesium deficiency are 1 metabolic factors that affect the absorption distribution and excretion of this mineral 2 disease and therapy 3 physiologic states that increase requirements for nutrients and 4 nutritional imbalances Excesses of nutrients that interfere with the absorption or increase the excretion of magnesium such as fat phosphate sugar and vitamin D can contribute to long lasting relative magnesium deficiency All have been implicated in several of the diseases considered in this book Whether their influence on the need for magnesium is a common denominator remains to be investigated further      **Noninvasive Imaging of Cardiac Metabolism** Ernst E. van der Wall,2012-12-06 F J Th WACKERS Metabolic imaging The future of cardiovascular nuclear imaging Since cardiovascular nuclear imaging emerged as a new subspecialty in the mid 1970s the field has gone through an explosive growth Radionuclide techniques became readily recognized as important new diagnostic aids in the armamentarium of the clinical cardiologist Initially

cardiovascular nuclear imaging focused on static myocardial imaging using either thallium 201 or technetium 99m pyrophosphate for diagnosing acute myocardial infarction Shortly thereafter multigated equilibrium radionuclide angiocardigraphy became the most widely used noninvasive method for assessing cardiac function Furthermore attention and clinical application shifted towards the use of radionuclide techniques in conjunction with exercise testing either with thallium 201 myocardial perfusion imaging or technetium 99m left ventricular function studies The future of cardiovascular nuclear imaging appeared exciting and promising However around 1980 pessimists predicted the premature demise of cardiovascular nuclear imaging with the introduction of digital subtraction angiography and nuclear magnetic resonance imaging These doomsayers have been proven wrong in 1985 cardiovascular nuclear imaging is thriving and in many centers even expanding Although digital subtraction angiography and magnetic resonance imaging provided exquisite anatomic detail for practical evaluation of patients with ischemic heart disease in the Coronary Care Unit or exercise laboratory nuclear techniques appeared to be more practical

**New Actions of Parathyroid Hormone** Shaul G. Massry, Takuo Fujita, 2012-12-06 Shaul G Massry Division of Nephrology The University of Southern California School of Medicine Los Angeles California In the last two decades evidence has accumulated indicating that parathyroid hormone may exert a multitude of effects on many cells and a variety of organs beyond its classical targets the kidney and the bone These efforts have been spearheaded by nephrologists The interest of this group of clinicians scientists stems from the fact that patients with renal failure have secondary hyperparathyroidism and markedly elevated blood levels of PTH 1 2 If this hormone does act on various organs it becomes plausible that excess blood levels of PTH may be harmful in these patients Indeed in an Editorial published in 1977 Massry suggested that the elevated blood levels of PTH in patients with renal failure may exert deleterious effects on many systems and as such may participate in the genesis of many of the manifestations of the uremic syndrome 3 Thus the essence of the Massry hypothesis is the notion that PTH may act as a major uremic toxin The search for uremic toxins did not yield successful results In the last three decades many compounds have been implicated as uremic toxins However a cause and effect relationship between these compounds and the manifestations of the uremic syndrome has not been established in most cases

*NIH Publication*, 1980 *Current Catalog* National Library of Medicine (U.S.), 1983 First multi year cumulation covers six years 1965 70 *Medical Research in the Veterans' Administration* United States. Veterans Administration, 1971 *Medical Research in the Veterans Administration*, 1974 *Cardiovascular Toxicology* Bob Sproull, Bob Nelson, 2001-07-19 Acosta's popular volume provides information on cardiovascular toxicology for clinicians public health officials industrial and experimental toxicologists as well other interested professionals This new edition highlights major advancements on the molecular aspects of toxicity to the cardiovascular system including genomics information where a

**Sudden Coronary Death** V. Manninen, P. I. Halonen, 1978-10-11 *Physical Activity and Coronary Heart Disease* V. Manninen, P. I. Halonen, 1976-09-14 **Chemical Sensitivity** William J. Rea, 2023-05-09 The volumes that

comprise Chemical Sensitivity are the first major scientific books to be published on chemical sensitivity a growing world wide health problem These volumes present clinical experiences in diagnosing and treating chemical sensitivity in over 20 000 patients under controlled conditions     Low Calorie and Special Dietary Foods B.K. Dwivedi,2018-01-18 This book is based on the papers presented at the Symposium on Low Calorie and Special Dietary Foods at the annual meeting of the Institute of Food Technologies in Anaheim California on June 8 1976     *Myocardial Metabolism* International Study Group for Research in Cardiac Metabolism,1973

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