

Preface

Today, noninfectious diseases have largely supplanted infectious diseases as the primary cause of morbidity and mortality in the developed and developing worlds. The diseases that now occupy center stage are age- and lifestyle-associated. They have proven to be remarkably difficult to treat let alone cure. The disorders do not have discernable Achilles heels and to-date few if any magic bullets have been found.

These challenges and difficulties are reflected in the extraordinary efforts now underway around the world to understand the underlying causes and find ways of effectively combating these diseases. The efforts cut across multiple disciplines and have led to the creation of entirely new subfields within the traditional physics, chemistry, biology, engineering, and computer science communities. Many of these newer fields are by now long- and well-established, and their names well known to everyone. Their combined goal is nothing less than a full understanding of how the human body works.

This goal is the greatest of the grand challenges in science today. It requires understanding at multiple spatial and temporal levels from molecules to cells to tissues and organs to systems. It requires that this understanding be quantitative and describe in mechanistic detail how the different parts and components work together. The study of diseases and their disease states are an essential part of the endeavor – the failures and breakdowns in the body reveal a great deal about how the body works and, in turn, understanding the workings provides the needed underpinnings for devising ways to treat and eventually find cures for the diseases.

Three categories of noninfectious diseases predominate. The first are the metabolic disorders. These are associated with changes in lifestyle that lead to obesity. The two most prominent disorders within this category are type 2 diabetes and atherosclerosis. The second major grouping is the cancers. These range from metastasis-prone solid tumors to the leukemias. The third class consists of the neurodegenerative diseases. The most prominent of these are Alzheimer's disease and Parkinson's disease.

Each of these disease categories is associated with a particular group of target tissues. Type 2 diabetes affects tissues that manage nutrients and energy resources. Atherosclerosis deals with endothelial cells that line medium and

large blood vessels. Solid tumors are prone to emerge from epithelia that must repair and replicate from time to time. Neurodegenerative disorders emerge, of course, from neurons, but interestingly, each disorder targets a specific type of neuron and not others. The tissue selectivity of these diseases arises from the properties and associated functions of the cell types that render them particularly susceptible to the causal agents. At the same time, and most significantly, these diseases share many common features. Among these are inflammation, altered metabolism, impaired oxidative balance, misfolded proteins, and dysregulated signaling. These manifest themselves in the different tissues in ways that reflect their aforementioned specific functions and properties.

The goal of this text is to present an up-to-date exploration of these three disease categories and their diseases that accurately reflects the multidisciplinary character and findings of ongoing research activities. In doing so, particular attention and emphasis are given to models and explanations that supply mechanistic details at the molecular level of how a certain process or set of events occurs thereby addressing “how” questions. The aim is to let each disease “tell its own story” in a way that brings out the unique character of each disease and in the process reveals something important on how the body works. Once that is done and understood, one can appreciate the common features that ultimately unite the diseases, and may eventually give rise to a unified “theory of the disease state” and how to prevent such states from being occupied for appreciable amounts of time.

The discourse will, by its very nature, encompass a set of models or exemplars on how the diseases under discussion might develop and progress. The models are not intended to be all inclusive, that is, they cannot include everything known or posited as having a possible role in a given disease. Such models by including everything usually end up by explaining nothing. Models that do not provide the mechanistic information on how something is happening are of dubious utility in an endeavor of this type and these have been avoided as well. The selections of what to include and what not to include, are, as always, subject to limitations on the part of the writer. Apologies are therefore advanced to those researchers who feel either neglected or misrepresented. The faults are not theirs but mine.

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