DRUGS AND THE PHARMACEUTICAL SCIENCES VOLUME 13

Orphan Drugs

edited by

Fred E. Karch

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Fred E. Karch, M.D.

Center for the Study of Drug Development
University of Rochester School of Medicine and Dentistry
Rochester, New York

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Orphan Drugs

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To all who suffer needlessly
while waiting for their orphan drug

Preface

What are "Orphan Drugs"? This is the name for a group of drugs which could save lives and alleviate suffering if they were made available. These drugs have already been discovered and could assist in the potential treatment of a wide range of illnesses such as: congestive heart failure, kidney infections, shock, gallstones, and epilepsy.

The question is: "Why aren't these drugs available?" There are many different reasons for this: money, insufficient market, commercial viability, patent problems, federal funding, etc.

This book presents case histories of six acknowledged orphan drugs, which illustrate the scope and complexity of the problem. These drugs cover: cardiovascular disease, disabling neurologic disorders, inherited metabolic diseases, chronic pulmonary disorders, and the treatment of chronic pain. By examining the individual cases, we can identify many of the factors that have kept these drugs from being developed.

In addition to discussing the orphan drugs themselves, we have also examined some of the efforts that have been made by federal agencies and the pharmaceutical industry to help adopt the orphan drugs.

Although much has been done, many valuable therapies remain undeveloped and unavailable. The last chapter discusses what can be done to help develop these drugs. Too many patients suffer needlessly while waiting for their orphan drugs.

Fred E. Karch

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Contributors

Thomas H. Althuis, Ph.D. Manager, Scientific Affairs, Public Affairs Division, Pfizer, Inc., New York, New York

Stephen L. De Felice, M.D. President, Bio/Basics International, New York, New York; Chairman, The Foundation for Innovative Medicine, New York, New York

Sandra L. Ford Staff Assistant, Parasitic Diseases Division, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia

Leon I. Goldberg, M.D., Ph.D. Professor, Department of Pharmacological and Physiological Sciences and Department of Medicine, and Chairman, Committee on Clinical Pharmacology, The University of Chicago, Chicago, Illinois

Fred E. Karch, M.D. Clinical Assistant Professor, Department of Pharmacology and Toxicology and Department of Medicine, and The Center for the Study of Drug Development, University of Rochester School of Medicine and Dentistry, Rochester, New York

Ronald L. Krall, M.D. Assistant Professor, Department of Neurology, University of Rochester School of Medicine and Dentistry, Rochester, New York

Louis Lasagna, M.D. Chairman, The Center for the Study of Drug Development, and Professor, Department of Pharmacology and Toxicology and Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York

Thomas H. Maren, M.D. Graduate Research Professor, Department of Pharmacology and Therapeutics, University of Florida College of Medicine, Gainesville, Florida

James F. Stubbins, Ph.D. Professor, Department of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia

Melvin H. Van Woert, M.D. Professor, Department of Neurology and Department of Pharmacology, Mount Sinai School of Medicine, New York, New York

J. M. Walshe, Sc.D., F.R.C.P. Reader in Metabolic Disease, Department of Medicine, University of Cambridge, Cambridge, England, United Kingdom; Honorary Consultant Physician, Addenbrooke's Hospital, Cambridge, England, United Kingdom

John F. Zaroslinski, Ph.D.* Vice President, Research and Development, Arnar-Stone Laboratories Division, American Hospital Supply Corporation, McGaw Park, Illinois

C. Gordon Zubrod, M.D. Director, Comprehensive Cancer Center for the State of Florida, University of Miami School of Medicine, Miami, Florida

**Present affiliation*: Adjunct Professor, Department of Pharmacology, Stritch School of Medicine, Loyola University, Maywood, Illinois

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Why Orphan Drugs?

Fred E. Karch, M.D.
University of Rochester
School of Medicine and Dentistry
Rochester, New York

An Introduction

Mary is 27, and she is dying. When she was 14 she began having trouble speaking. Over the last several years her voice has become weak, her speech slurred, and her vision blurred. She has trouble swallowing and food sticks in her throat, often choking her. Mary's hands shake, her shoulders move in uncoordinated jerks, and she has trouble walking. As the day progresses her symptoms get worse. Medications have not stopped her gradual deterioration. Mary and her husband have almost given up. But a new drug was discovered recently that might control Mary's disease. Unfortunately, she cannot get the drug. None of the drug manufacturers have been willing to develop it, and it is simply not available. Without this new drug, Mary's future is bleak.

Despite our enormous national expenditure for medical care and medical research, we still cannot cure most illnesses. These incurable diseases inflict pain and cause physical disability, suffering, and death. The emotional drain on patients and their families is severe. But it is so much worse when they know that promising new drugs have been discovered but may never be available to them. What cruel torment it is to add to a patient's affliction. A potential treatment has been discovered, but the drug is not available because pharmaceutical manufacturers and government agencies are not sufficiently interested in developing it. Such drugs have been called "orphan drugs"–potentially valuable new agents that have not been developed for medical use. Without the support of private industry or federal agencies these compounds cannot be fully tested and made available to treat afflicted patients.

Why haven't these orphan drugs been developed? There are almost as many different answers to that question as there are orphan drugs.

A local merchant recently told me how he envisioned drug development. Pharmacologists and clinicians at major medical centers work in their laboratories discovering the new wonder drugs. When they succeed, a drug company quickly manufacturers the drug, and everyone benefits. The patients get the new drug, the manufacturer makes a profit, and the scientists are recognized for their achievements. His vision was of dedicated Arrowsmiths working in small laboratories for the good of humankind.

My friend's view, aside from being simplistic, is far off the mark for most drugs, which are usually discovered by large commercial drug companies. Orphan drugs, however, fit his image a little better. Unfortunately, after the scientist makes a discovery, all too often that is the end of the line.

The scientist cannot get a pharmaceutical manufacturer to make the investment to develop the new drug. Some drugs are natural products that

cannot be patented. Others have an apparently small market, and commercial manufacturers cannot justify the development expense to their board of directors and stockholders. Even when a pharmaceutical company does attempt to develop an orphan, the inevitably limited resources are committed primarily to economically more important drugs. The orphan may not get the attention it needs to reach the market.

Getting money from federal agencies such as the National Institutes of Health may be even harder. The government sees drug development primarily as a private commercial effort that should not be underwritten with public funds.

If the scientist is still willing to fight for the drug after these frustrating encounters with industry and government agencies, perhaps a university or a private foundation can be convinced to provide research support. The school or foundation might share in the subsequent financial success.

One orphan drug did get a commitment from a major university, and its future seemed bright. A well-known expert gave the drug a favorable evaluation in a review for a major journal. Then the storm clouds rolled in. The university's legal counsel was concerned that clinical studies might subject the school to product liability claims. Liability insurance was sought, but the $98,000 annual premium plus the risk of up to $500,000 additional cost (from deductibles) each year for the lifetime of each patient was too much for the university. Without insurance the orphan had to be abandoned again.

The bottom line, of course, is money. It has been estimated that in 1976 it cost over $50 million to develop a new drug in the United States (1). With inflation, that figure has undoubtedly been surpassed.

Why does it cost so much to develop a drug? Good scientific research is expensive, and before a drug can be marketed the federal Food and Drug Administration requires exhaustive research on its safety and effectiveness Years of clinical and laboratory research are needed to meet these stringent requirements. It seems that the United States has the strictest drug development regulations of any country, but other nations also have both governmental regulations and orphan drugs. Whether such stringent requirements are always necessary is another issue, but the cost of meeting these requirements is a significant factor in the desertion of some orphan drugs.

How many orphan drugs are there? Nobody really knows. Without considerable investment in original research, scientists cannot conduct the experiments to show that a new compound might be an effective drug. Without research data, the compound's potential is unknown, much as a baby's future is unknown at birth. With limited financial support, scientists may