

Drug Hypersensitivity

Drug Hyper— sensitivity

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Foreword

Drug hypersensitivity is a complex and still widely neglected topic. It is considered to be a difficult area of medicine, as many different drugs can cause hypersensitivity reactions, albeit each drug rather rarely. It can result in many different types of diseases, with unknown but presumably quite distinct pathomechanisms. Although almost every doctor has encountered some drug-allergic diseases, not many doctors have large experience with a certain drug and a certain type of drug hypersensitivity. As drug hypersensitivity characteristically appears unexpectedly, patient-oriented research is difficult. Because of its unpredictable nature it was distinguished from pharmacological reactions (type A) and termed a type-B reaction, whereby B was soon interpreted as meaning bizarre! These features did not contribute to making drug hypersensitivity a popular area of medicine or science, the chances of finding a breakthrough were simply considered to be too small.

Until now, most books on this topic have focused on epidemiological aspects and listed the drugs and their side effects, but the immune pathogenesis, its relation to the clinical features of drug hypersensitivity diseases, immunogenet-

ic aspects, animal models, new diagnostic possibilities, treatments and desensitizations have not been discussed in detail. This book tries to change this approach and tackles these areas. It covers epidemiology, pathogenesis, clinics and diagnosis of these diseases. It reaches from animal models to clinical chapters on how to approach a patient with drug allergy and how to desensitize him. The aim is to provide a general view on this topic – so that the practicing physician, the allergologist, the pharmacologist, the epidemiologist, the geneticist, the immunotoxicologist, the safety officer of a pharmaceutical company, and the scientist interested in interactions of small molecules with the immune system, etc., will find relevant information on this now rapidly evolving field of medicine.

This approach has become possible because during the last 10–15 years substantial development in this area has taken place. The important role of drug-specific T cells in these reactions has been deciphered; new animal models for certain forms of drug hypersensitivity diseases have been established, and new test systems have been developed to better define the incriminated drug. An important breakthrough was the identifica-

tion of extremely high HLA-B associations with certain drugs and diseases, which already results in effective prevention of some forms of drug hypersensitivity reactions.

The people interested in drug hypersensitivity come from many different areas. It is a truly interdisciplinary group which recently gained its own identity by holding two drug hypersensitivity meetings (in Bern 2004 and Liverpool 2006) where participants from different areas exchanged ideas. Most of the contributors to this book were present at these meetings and participated in the friendly but also hot discussions, not least because the group from Bern proposed a new concept on how T cells may be stimulated by drugs (pharmacological interaction with immune receptors, the p-i concept), which contradicted prevailing concepts quite radically. Future studies and results will show which of these ideas, which are also represented in the various chapters of this book, will prevail. If the p-i concept is confirmed (which I assume), we will have to learn what it means for the clinical symptoms, diagnosis and prediction of drug hypersensitivity reactions. But the impact of this new concept will go far beyond drug hypersensitivity alone, as it combines pharmacology with *antigen-specific* immu-

nology, and will therefore also influence other areas of research and medicine. In this case the idea of also seeing in a drug hypersensitivity reaction an unintended 'experiment' of the treating physician would be confirmed, and the only positive side of drug hypersensitivity would become apparent, namely that medicine and science could learn from drug hypersensitivity.

We need to approach these iatrogenic and thus often embarrassing diseases with an open mind, not frightened by the complexity of the issue, and not using its unpredictability as a permanent excuse to do nothing: It is not so much the disease which is embarrassing, but the handling of these unexpected side effects. Drug hypersensitivity reactions should and will become less bizarre and less frightening when physicians, scientists and the pharmaceutical industry work together to better understand these diseases.

I would like to thank the many contributors to this book, they did an excellent job. I am also very thankful to Karger Publishers, in particular Thomas Nold, and my secretary Franziska Mitton who helped me to organize this book.

Werner J. Pichler

Bern, November 2006