Achille Patrizio Caputi, Giuseppina Fava

Drugs and Laboratory Parameters

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Piazza Carlo Emanuele II, 19 – 10123 Torino – Italy
Tel. +39.011.566.02.58 - Fax +39.011.518.68.92
www.edizioniseed.it
info@edizioniseed.it

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by Achille Patrizio Caputi, Giuseppina Fava

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SUMMARY

PREFACE TO THE ENGLISH EDITION

Adverse drug reactions (ADR) are inevitable consequences of pharmacotherapy. The identification of a possible adverse event is the first step in a diagnosis of ADR. It is simpler to identify visible and symptomatic events, such as those affecting skin, than asymptomatic ones, as are usually changes in laboratory values. In addition, while skin could be considered as a classic system affected by ADRs, laboratory value changes are intrinsically more ambiguous, and may be less easy to recognise as being related to a drug treatment.

Most marketed drugs may cause a wide range of modifications to laboratory values that are mostly non-specific, and these may also be associated to a complication of the treated disease (e.g. diuretic-induced nephropathy vs. hypertensive nephropathy). Certain ADRs, however, may be expected in view of the drug indication. This is the case of medication acting on coagulation, such as warfarin or other vitamin K antagonists, which are expected to cause changes in laboratory parameters that could become severe, symptomatic, and even fatal if not adequately monitored. Therefore anomalies have every chance to be identified and managed. On the other hand, most medications do not require monitoring via periodic laboratory tests, and the identification of anomalous values, as well as differential diagnosis with other non-pharmacological causes could be more difficult.

In daily practice, clinicians prescribing drugs have in mind efficacy before safety. Even for a clinical pharmacologist, it is impossible to remember all the ADRs associated with a single drug. For this reason, tools supporting the daily activities of clinicians are needed, and this book moves in this direction. Whereas most books on ADRs and drug dictionaries go from the drug to the symptom or ADR, this book may be used when

faced with a laboratory test anomaly to rapidly identify what drugs may have or are known to be associated with this anomaly, thereby facilitating patient management. The inclusive nature of the information, collected from an overview of well-recognised data-sources concerning ADRs, and its layout make this book unique in terms of quality and, more importantly, utility for clinicians, helping them easily find information for the best management of their patients.

Dr. Francesco Salvo
Department of Pharmacology, University of Messina,
Messina, Italy

Prof. Nicholas Moore
Department of Pharmacology, University of Bordeaux,
Bordeaux, France

FOREWORD

During the last decade the importance of pharmacovigilance has increasingly grown. The word "pharmacovigilance" was proposed in the first half of the 1970s by a group of French pharmacologists and toxicologists to define all the activities aiming at promoting the "evaluation of the risk of adverse events potentially associated with drug administration."

The first step of pharmacovigilance is signal generation, i.e., the process that can identify possible new *adverse drug reactions* (ADRs). After a signal has been identified, other steps are required to confirm or repudiate the signal:

- hypothesis testing, i.e., processes that determine whether the signal does indeed indicate a new ADR, or whether it is false;
- hypothesis strengthening and preliminary evaluation of available data;
- evaluation, examination, and explanation of the signal.

Detection of ADRs is extremely important, since they represent a major health problem with many clinical consequences and high economic and social burdens. Unfortunately, in everyday practice there is a wide variation of potential risk factors associated with ADRs, and their recognition is still challenging. Signal detection based on spontaneous reporting is, in our opinion, absolutely essential, because it may generate rapid alerts and stimulate follow-up.

Even if ADRs are often associated with hypersensitivity reactions, clinical and laboratory parameters can also be considered as predictors for ADRs. A signal can therefore arise from abnormal results of diagnostic tests; these tests represent qualitative and quantitative descriptions of the physical-chemical state of the analysed system and its components, allowing

diagnosis, follow-up, screening, and response to drug administration.

Nonetheless the possibility of a drug-related variations of blood tests is seldom taken into consideration. The aim of this easy-to-read book is to help physicians in their routine interpretation of laboratory results, drawing their attention to the possibility that abnormal results may be drug-related.

The book describes the most common variations (increase/decrease) of blood parameters that can be caused by drug intake; such variations are classified on the basis of diagnostic criteria (organ/disease). Data have been derived and adapted mainly from three reference books [Bonardi 1995, Burlina 1987, and Covelli 2001], which, despite their publication dates, still represent authoritative references in this field. Other books have been consulted [Fava 2005, Federici 2003, and Nespoli 1975], and all the data have been updated on the basis of findings in the literature (i.e., articles published on PubMed) and dedicated websites (e.g., www.farmacovigilanza.org, www.micromedex.com, and www.RxList.com).

The functions of each blood parameter are schematically reported, together with the standard blood concentration and a list of the most common diseases for whose diagnosis that test is performed. Active principles are then listed, which can cause an increase or a decrease in that parameter. Standard concentrations here reported are taken from the reference books previously cited; it is essential, however, to remember that each laboratory fixes its own standard concentrations, and that therefore they may not correspond exactly with those reported here. The book concludes with two indexes, allowing research on both parameters and drugs.

This text is not intended as an exhaustive reference; it is quite impossible to obtain a complete list of all the parameters and all the drugs potentially responsible for variations, because of objective difficulties in finding material about this topic. The

book's main purpose is to provide an overview of the most common drugs potentially responsible for unexpected laboratory results, giving clinicians an insight into the risk of drug interference in laboratory testing.

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