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## The Dawn of Drug Safety

Myles D.B. Stephens. George Mann Publications: Eaton, Winchester, Hampshire SO21 1ES, UK. 2010 May. Hardback. 432 pages. ISBN 9780956087485

A Review by David Clark, East Taieri, New Zealand

The picture on the cover of this book sets the scene with Lee W. Gilbert's spectacular photograph 'Dawn, Tasman Sea', and the introduction to this fascinating and well researched book continues to develop the theme of the start of a new era in drug safety with two circular diagrams depicting lines of communication.

The first of these diagrams is headed "The Pharmacovigilance Cycle Pre-Thalidomide" and illustrates communication pathways between the patient and the 'health professional', with examples of the latter being listed as "wise woman, sage, witch, priest, apothecary, district nurse, physician". The second diagram, "The Pharmacovigilance Cycle Post-Thalidomide", illustrates current lines of communication in pharmacovigilance that have resulted from the thalidomide tragedy. It depicts interactions between the WHO and patient through 'national authorities', 'pharmaceutical companies' and 'health professionals'. The first diagram, "Communication Pre-Thalidomide", sums up the subject matter of this book: that is, an analysis of evidence relating to adverse effects of herbs and drugs prior to the thalidomide disaster.

The book is in four parts, with the first part containing a chronological account of the discovery, reporting and management of adverse reactions to medicines in the context of important medical events from the beginning of recorded time until 1961, when the thalidomide disaster resulted in permanent and dramatic changes to the approach to drug safety. This part, headed "Chronicles of Drug Safety", commences with an introductory account of the pre-biblical era of substance use, including alchemy, which was "born out of superstition and magic". The first chapter of Part 1 includes discussion of sources of information on this. It is followed with an account of evidence for use of herbal remedies in the stone age to the middle palaeolithic age (180 000–22 000 BC), the neolithic age (7000 BC), the bronze age (2300–600 BC), the iron age (1200 BC–400 AD) and the Roman age (circa 600–23 BC).

A chapter containing an account of the 'biblical era' up until 1200 AD follows and this includes an extensive account of medical writers and their philosophies at the time and a brief listing of the ways in which drugs might be adulterated. The following chapters discuss such topics as "The Age of Herbals", "Dispensatories" (which contains accounts of early non-herbal remedies), the role and history of apothecaries and important developments from the 16th through to the 19th centuries. In a chapter on developments in the 19th century, developments in areas such as "Placebo-Controlled Clinical Trials", "Disease Nomenclature", "Drug Interactions", "Health Insurance Schemes" and the setting up of "Adverse Reaction Committees" are discussed.

Part 1 concludes with a chapter on the 20th century, which includes examples of the recognition of allergic reactions and describes various acts that were passed and bodies that were formed (such as the Medical Research Council) to help ensure purity and safety of vaccines and drugs. Discussion of the term 'poison' makes the often-overlooked maxim that whether a substance is a poison is a question of dose. Other important areas discussed are the strength of evidence that an adverse event was caused by a drug, books on the side effects and abuse of drugs, and a brief comment on regulations and laws pertaining to drugs.

Part 2, headed "The Analysis of Marker Drugs" is an analysis of six drugs (hellebore, henbane, mercury, opium, aspirin [acetylsalicylic acid] and streptomycin) representing typical medicines used over 3000 years. In this part, analyses of the dates when the adverse drug reactions (ADRs) were reported first and the description of the ADR indicates the development of early processes of pharmacovigilance over time. Tables are included to provide a listing of the ADRs recorded. However, it is pointed out

that early reports were often not specific. Part 3 of this book, ''Regulatory Responses to Adverse Reactions'', is an analysis of the 50 drugs that had been on the market prior to 1960 and which have been either withdrawn or restricted because of one or more adverse reaction(s).

The final part of the book, Part 4 ''Discussion'', comments on the findings of the extensive and detailed investigations that the author has carried out in writing this book.

In a brief review, it is not possible to do justice to the meticulous research that has been carried out in accumulating the information that is covered in this book. The account of the lead-up to the marketing of thalidomide makes frightening reading: a tragedy waiting to happen. In many ways thalidomide appeared to be the ideal sedative: it could be given in high doses with no apparent toxic effects. Unlike the sedatives available at the time, barbiturates and early benzodiazapines, there was minimal evidence in pre-marketing trials that thalidomide caused dependence, and people who tried to commit suicide with overdoses of thalidomide were unsuccessful. There was concern in some quarters that there may be an association with birth defects; however, the first report of an association with phocomelia was not until November 1961. By this time, many doctors had been given thalidomide samples to provide their patients with the latest in sedatives that did not lead to dependence.

The author of this review has first-hand experience with the nonchalant attitude to thalidomide. He was serving an apprenticeship in pharmacy in the early 1960s when a sales person, known then as a 'drug detailer', placed samples of thalidomide in cardboard packs on the counter to give as a sedative to patients who needed something to settle them down. He emphasised the 'safety' of the drug, due to the lack of potential for dependence, compared with barbiturates and the early benzodiazapines. The thalidomide tragedy was yet to happen.

Overall, this is an impressive book that provides a great deal of information on the recognition of ADRs prior to the thalidomide disaster. The analyses of selected marker drugs, and the adverse reactions to these, are meticulously researched. Readers with an interest in the development of ADR reporting and the history of safety in the use of drugs will find this a valuable and fascinating account of the recognition of ADRs prior to the thalidomide disaster. It is highly recommended that *The Dawn of Drug Safety* should be on the library shelves of all pharmacovigilance centres and tertiary institutions teaching courses in health sciences.

The following details have been supplied by the author:

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Correspondence: Associate Professor *David Clark*, Honorary Associate Professor, Department of Pharmacology & Toxicology, School of Medical Sciences, University of Otago, P.O. Box 913, Dunedin, New Zealand.
E-mail: david.wj.clark@gmail.com