

Antiepileptic Drugs and Pregnancy

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A Guide for Prescribers

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Preface

A prospective reader might well wonder why, at the present time, anyone would devote a monograph to such a seemingly limited topic as that of antiepileptic drugs and pregnancy. This is particularly so when it is generally accepted that, as far as possible, the use of therapeutic drugs should be avoided in pregnant women. This latter belief originated some half a century ago when thalidomide use in pregnant women was recognised to be responsible for the development of foetal malformations and when the prescription of stilbestrol for threatened miscarriage was found to result in gynaecological malignancies in the daughters of the women so treated. The short answer to the question posed above is that the use of antiepileptic drug therapy in pregnancy continues to be perhaps the most frequently encountered situation in which the use of therapeutic drugs in pregnant women appears clinically and ethically justified. As a result of the virtual embargo on the unnecessary use of therapeutic drugs in pregnant women, there is not a great deal of information available regarding the possible effects that pregnancy might have on the body's handling of these drugs or on the effect that these drugs may have on pregnant women and their foetuses. Therefore, the availability of information about these matters in relation to antiepileptic drugs, necessarily gathered in opportunistic studies rather than in deliberate controlled investigations, offers the possibility of obtaining knowledge from which principles can be derived that may prove more widely applicable in the future to new drugs as they become available and their possible use in human pregnancy is considered.

Over the course of almost half a century of such piecemeal accumulation of information concerning antiepileptic drugs in human pregnancy, sufficient relevant material appears to have been amassed for a reasonably systematic and probably fairly complete account of the current situation to be possible. It is hoped that such an account may prove of interest to those who manage patients with epilepsy, particularly neurologists and general physicians, and also obstetricians, and that it may also contain material that would also be useful to basic and clinical pharmacologists and to other medical professionals who appear to be increasingly using antiepileptic drugs to treat disorders other than epilepsy, in particular certain psychiatric illnesses.

All of the illustrations used in this book have been prepared by one or any of the authors and, except for the diagrams of metabolic pathways, are based on personal data. Where this material has been published previously, it has appeared in journals whose publishers do not require explicit permission for reproduction by the authors of illustrations that they have prepared. However, nearly all the graphs in this book have been redrawn to bring them into a common format. At first sight, some may appear similar to previously published illustrations, but the figures have been redrawn to include the additional data available in the Australian Pregnancy Register at the end of 2014.

A significant portion of the data presented in this volume has emanated from an ongoing collaboration between the authors over a period of more than 40 years. During the past 15 years, this collaboration has involved the collection and analysis of the prospective data related to the use of antiepileptic drugs in the management of women with epilepsy that are collected in the Australian Register of Antiepileptic Drugs in Pregnancy. In relation to the latter endeavour, we are greatly indebted to our colleagues in Australia, viz. TJ O'Brien, CM Lander, J Graham, A Hitchcock, A Roten Wood and C Nadebaum for their excellent and continuing participation in, and support of, the activities of the Register. Our thanks are due also to European colleagues, T Tomson, D Battino, D Lindhout, A Sabers, J Craig, D Bonnizzoni and E Perucca, S Thomas, for the tremendous collaborative facility they have created in the EURAP registry. We also wish to acknowledge support for the Australian Register from a variety of sources including the Australian National Health and Medical Research Council, the Epilepsy Society of Australia, the Royal Melbourne Hospital Neuroscience Foundation and the pharmaceutical industry, including the firms of Sanofi, Sci-Gen, UCB, Genzyme, Janssen, Eisai, Novartis and previously Pfizer, Glaxo, Roche, Schering, Marion Merrell Dow, Hoechst and CSL.

Thanks are also due to Simon Raoul Vajda for computer-related technical assistance and to Margaret Eadie for general support of the work.

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