

# Cardiovascular adverse effects of phenytoin

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**Abstract** Phenytoin is an established drug in the treatment of acute repetitive seizures and status epilepticus. One of its main advantages over benzodiazepines is the less sedative effect. However, the possibility of cardiovascular adverse effects with the intravenous use of phenytoin cause a reluctance to its usage, and this has lead to a search for safer anticonvulsant drugs. In this study, we aimed to review the studies which evaluated the safety of phenytoin with respect to cardiovascular adverse effects. The original clinical trials and case reports listed in PUBMED in English language between the years of 1946–2014 were evaluated. As the key words, “phenytoin, diphenylhydantoin, epilepsy, seizure, cardiac toxicity, asystole, arrhythmia, respiratory arrest, hypotension, death” were used. Thirty-two clinical trials and ten case reports were identified. In the case reports, a rapid infusion rate ( $>50$  mg/min) of phenytoin appeared as the major cause of increased mortality. In contrast, no serious cardiovascular adverse effects leading to death were met in the clinical trials which applied the recommended infusion rate and dosages. An infusion rate of 50 mg/min was reported to be safe for young patients. For old patients and patients with a cardiovascular co-morbidity, a slower infusion rate was recommended with a careful follow-up of heart rhythm and blood pressure. No cardiovascular adverse effect was reported in oral phenytoin overdoses except one case with a very high serum phenytoin level and hypoalbuminemia.

Phenytoin is an effective and well tolerated drug in the treatment of epilepsy. Intravenous phenytoin is safe when given at recommended infusion rates and doses.

**Keywords** Epilepsy · Phenytoin · Cardiovascular adverse effects · Arrhythmia · Death

## Background and aim

Phenytoin was introduced as an epileptic drug in 1938 and later was also used as an antiarrhythmic drug in cardiology. Currently, its usage as antiarrhythmic purpose is abandoned, but its oral and intravenous (IV) forms still reserves their importance in the treatment of epilepsy. Phenytoin is one of the four drugs which are declared by ILAE to have a level A efficacy in the treatment of focal epilepsy [1]. Moreover, the use of IV phenytoin just after diazepam administration is also recommended as a level A drug as an alternative to IV lorazepam in the treatment of status epilepticus (SE) [2]. Some serious adverse effects of IV phenytoin such as cardiac arrhythmias, hypotension, respiratory arrest and related deaths were historically reported particularly in the field of cardiology [3–7]. These unfavorable reports cause a hesitation in the usage of IV phenytoin. The recommended slowed infusion rates and cardiac monitoring during the infusion as precaution have also made the IV phenytoin administration difficult. Meanwhile, the new antiepileptic drugs with less (cardiac) adverse effects try to replace phenytoin in the epilepsy treatment although they are not more effective than phenytoin [2, 8–19].

Here, we review the safety of IV phenytoin administration in the epilepsy treatment by evaluating the available studies and case reports containing data about the cardiovascular adverse effects of phenytoin.

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# Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body

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## **Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body:**

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Medicus ,1972      *Epilepsy Bibliography, 1950-1975* J. Kiffin Penry,1976 1771 entries to worldwide literature mostly journal articles Intended as source of current published works on epilepsy also serves as cumulative index to Epilepsy abstracts v 1 9 1967 1976 Classified arrangement under 9 broad headings e g Seizures Etiology and Treatment Entries include bibliographical information with foreign language titles also in English and Epilepsy abstracts citations Keyword subject indexes      *Paperbound Books in Print* ,1992      **Hospital Formulary and Compendium of Useful Information** University of California (1868-1952),      **Subject Guide to Books in Print** ,1991      **The Failed Back Syndrome** Harold A. Wilkinson,2012-12-06 In the eight years since the first edition of this book several marvelous technical advances have become available clinically for the care of patients with failed back syndromes High resolution MRI scans three dimension al CT scans and percutaneous discectomy are notable technological ad vances Overall however the problem of the failed back remains as complex and poorly understood as ever A discouraging amount of what we claim to be our knowledge of the pathophysiology and appropriate therapy for the complex of disorders that constitute the failed back syndrome re mains unvalidated by careful scientific study 1 The discussions of patho physiology diagnosis and therapy put forth in the first edition for the most part remain equally as valid or as controversial as they were eight years ago The first edition was well received by numerous physicians and other health care givers from a variety of disciplines and through them the book seems to have contributed usefully to many of those who suffer the unpleasant mal adies of the failed back I hope this second edition will likewise prove to be a positive contribution The timing of the publication of this second edition is significant in several ways in the context of the current medicolegal climate in the United States      *Small Animal Clinical Pharmacology* Jill E. Maddison,Stephen W. Page,David B. Church,2008 Small Animal Clinical Pharmacology is a practical clinically oriented pharmacology text designed to provide the veterinary student and practitioner with all the relevant information needed when designing drug treatment regimens for pets in small animal veterinary practice Comprehensively updated and revised the second edition of this core text covers essential new information on drugs used in the management of a range of presenting conditions including heart disease and cardiac arrhythmias For the second edition new authors superb new illustrations and a second colour have all been introduced With its unique approach combining a thorough understanding of the pharmacological action of drugs with a basic understanding of the relevant physiology and pathophysiology of systems and tissues affected Small Animal Clinical Pharmacology continues to be an indispensable book for all veterinary students and practitioners Organised by drug class in a uniform and detailed structure which means it is easy to locate key information on dose rates routes of administration drug interactions and special considerations at a glance Key chapters based around treatment of disorders of particular body systems eg cardiovascular and thyroid disorders Essential introductory chapters covering pharmacokinetics general pharmacological principles and adverse reactions for a thorough basic grounding in the subject All authors are experienced clinicians and recognised experts in their field who bring a down to earth and practical

approach to the text      Clinical Pharmacology of Anti-Epileptic Drugs H. Schneider,D. Janz,C. Gardner - Thorpe,H. Meinardi,A. L. Sherwin,2012-12-06 He who is faithfully analysing epi lepsy is doing far more than studying epilepsy Hughlings Jackson Modifying this well known statement by Jackson one could say today He who is faithfully analysing anti epileptic drugs is doing far more than studying anti epileptic drugs For these drugs not only serve to prevent epileptic fits and thus advance the treatment of epilepsy they are also effective in the treatment of cardiac arrhythmias and trigeminal neuralgia Furthermore clinical pharmacologists consider anti epi leptic drugs as model drugs in pharmacokinetics and pharmacodynamics since reliable methods are available for their determination and their effects and side effects can be defined The methods of estimating of drugs in body fluids provide a tool that enables us to throw light on many obscure relationships in pharmaceutical treatment Now that we can study the pharmacokinetics and interaction of drugs in man many hypotheses based on clinical experience alone may well be eliminated or corroborated The grow ing body of knowledge will make us more careful about the administration of drugs in combination Now that we can study how biological parameters interfere with drug action we may perhaps proceed to the scientific analysis of many clinical observations that suggest the importance of such factors as age sex menstrual cycle pregnancy fever diet stress sport climate and altitude

**Cerebrovascular Bibliography** ,1968      Talking Back To Ritalin Peter Breggin,2007-10-10 Millions of children take Ritalin for Attention Deficit Hyperactivity Disorder The drug s manufacturer Novartis claims that Ritalin is the solution to this widespread problem But hidden behind the well oiled public relations machine is a potentially devastating reality children are being given a drug that can cause the same bad effects as amphetamine and cocaine including behavioral disorders growth suppression neurological tics agitation addiction and psychosis Talking Back to Ritalin uncovers these and other startling facts and translates the research findings for parents and doctors alike An advocate for education not medication Dr Breggin empowers parents to channel distracted disenchanted and energetic children into powerful confident and brilliant members of the family and society      *Clinical Pharmacology in Dental Practice* Richard L. Wynn,Barbara Requa-Clark,1983

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## **Table of Contents Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body**

1. Understanding the eBook Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - The Rise of Digital Reading Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Advantages of eBooks Over Traditional Books
2. Identifying Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - User-Friendly Interface
4. Exploring eBook Recommendations from Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Personalized Recommendations
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body User Reviews and Ratings
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body and Bestseller Lists
5. Accessing Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body Free and Paid eBooks
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body Public Domain eBooks
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body eBook Subscription Services
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body Budget-Friendly Options

6. Navigating Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body eBook Formats
  - ePub, PDF, MOBI, and More
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body Compatibility with Devices
  - Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body Enhanced eBook Features
7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Highlighting and Note-Taking Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Interactive Elements Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
8. Staying Engaged with Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
9. Balancing eBooks and Physical Books Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
11. Cultivating a Reading Routine Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Setting Reading Goals Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Fact-Checking eBook Content of Phenytoin Dilantin Diphenylhydantoin And Its Adverse Effects In The Human Body
  - Distinguishing Credible Sources

13. Promoting Lifelong Learning
  - Utilizing eBooks for Skill Development
  - Exploring Educational eBooks
14. Embracing eBook Trends
  - Integration of Multimedia Elements
  - Interactive and Gamified eBooks

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