

Immunotoxicology And Immunopharmacology

Considerable scientific and political interest has been expressed, paralleling public concern about the effects of chemicals on the immune system and the implications of those effects for health. Coupled with speculation about the magnitude and extent of the problem is discussion of needs for predictive testing and regulatory control measures. The first international seminar on the immunological system as a target for toxic damage was held in Luxembourg in 1984. It was organized by the International Programme on Chemical Safety (United Nations Environment Programme-International Labour Office World Health Organization) and the Commission of the European Communities with the support of the US Environmental Protection Agency and the National Institute of Environmental Health Sciences (USA) and the participation of the International Society of Immunopharmacology. In view of the perceived importance of immunotoxicity, it was considered necessary to organize a follow-up meeting. Thus, an international workshop on the immunotoxicity of metals and immunotoxicology was held in Hanover, Federal Republic of Germany, on 6-10 November 1989. This textbook provides a unique support in gaining essential knowledge on the immune response, its diagnosis and its modification by drugs and chemicals. The first section of the book, covering a basic introduction to immunology and its relevance for human disease, has been updated to accommodate new immunological concepts. The second section on immunodiagnosics has been further expanded to describe widely used molecular techniques and is followed by a systematic coverage of drugs affecting the immune system, revised to cover recent developments. The book concludes with a chapter on immunotoxicology. This third edition continues the unique format dealing with four related topics in a single volume, obviating the need to refer to several different textbooks. New aids to the reader include a two-column format, glossaries of technical terms and appendix reference tables. The emphasis on illustrations is maintained from the first edition.

Advances in Immunopharmacology documents the proceedings of the First International Conference on Immunopharmacology held in Brighton, England, in July 1980. The volume contains 60 papers organized into 10 parts. The papers in Part I examine the pharmacology of immunotherapeutic drugs and immunotoxicology. Part II presents studies on thymic hormones. Part III is devoted to immunopharmacologic approaches to diseases other than cancer. Part IV deals with mechanisms of chemotaxis degranulation and microbicidal action. Part V focuses on cancer immunopharmacology

and immunotherapy while Part VI covers the mechanisms of inflammatory and allergic processes. Part VII takes up the immune testing of the actions of immunotherapeutic agents. Part VIII discusses prostaglandins and macrophage suppression. Part IX is devoted to selected topics such as mechanism of action of soluble immune response suppressor and new approaches to the therapy of allergic diseases. Part X presents discussions during the therapy communication sessions.

Clinical Environmental Health and Toxic Exposures

Introduction To Immunotoxicology

Zinc special feature

Supplements

Immunotoxicity of Metals and Immunotoxicology

Information Resources in Toxicology, Third Edition is a sourcebook for anyone who needs to know where to find toxicology information. It provides an up-to-date selective guide to a large variety of sources--books, journals, organizations, audiovisuals, internet and electronic sources, and more. For the Third Edition, the editors have selected, organized, and updated the most relevant information available. New information on grants and other funding opportunities, physical hazards, patent literature, and technical reports have also been added. This comprehensive, time-saving tool is ideal for toxicologists, pharmacologists, drug companies, testing labs, libraries, poison control centers, physicians, legal and regulatory professionals, and chemists. Serves as an all-in-one resource for toxicology information New edition includes information on publishers, grants and other funding opportunities, physical hazards, patent literature, and technical reports Updated to include the latest internet and electronic sources, e-mail addresses, etc. Provides valuable data about the new fields that have emerged within toxicological research; namely, the biochemical, cellular, molecular, and genetic aspects

The second edition of this text has been revised and refocused to reflect the transformation of immunotoxicology from a subdiscipline of toxicology to an independent area of research that can best be described as "environmental immunology." New chapters discuss the role of immune mediators in liver, lung, and skin toxicity, in regulating chemical- metabolizing enzymes, and in the immunosuppression produced by ultraviolet light. More emphasis is placed on the clinical consequences of immunotoxicity, as well as the interpretation of experimental data for predicting, human health risk.; The second edition is divided into three major sections: immunosuppression, autoimmunity, and hypersensitivity. This new organization of the text allows for a more thorough treatment of these phenomena, with greater attention to test methods, theoretical considerations, and clinical implications. The book

includes many chapters on specific environmental agents, therapeutic drugs, biological agents, and drugs of abuse, as well as on immune-mediated toxicity in specific organ systems. This volume is based on the program of the International Conference on Drugs of Abuse, Immunity and Immunodeficiency held in Clearwater Beach, Florida. It was sponsored by the University of South Florida College of Medicine with the support of the National Institute on Drug Abuse. During the past few decades, drugs of abuse, including marijuana, cocaine, opiates and alcohol, have been studied by biomedical scientists in terms of the systemic effects of the drugs as well as alterations in neurophysiology and the psychology. More recently, the scope of such investigations has been broadened to include alterations within the immune system, and the influence of altered immunity on physiological and psychological consequences of drug abuse. In this regard, participants in the Clearwater Beach conference provided new information concerning both basic and clinical aspects of drugs of abuse and immunity, especially immunodeficiency. Advances have been made in recent years in understanding the nature and mechanisms regulating the immune response and the mechanisms by which drugs may influence immune responses. In particular, the emergence of psychoneuroimmunology as a new discipline has heightened interest in immune responses influenced by psychoactive drugs. This has resulted in interdisciplinary investigations involving clinical and basic scientists including microbiologists, immunologists, physiologists, psychiatrists, oncologists and others. The recreational use of the above mentioned drugs by large numbers of individuals has aroused serious concern about the consequences of this activity.

Drugs of Abuse, Immunity, and Immunodeficiency

History of Immunotoxicology

Preclinical Methods for Detecting the Potential Hypersensitivity of Pharmaceuticals : Divonne-les-Bains (France), 4-6 October 1999

Immunopharmacology

Minisymposium 1 : 21st National Meeting : Abstracts

Chronic diseases are the leading cause of deaths worldwide and according to the World Economics Council and the Harvard School of Public Health, the cost of chronic diseases is expected to reach a staggering 48% of global gross domestic product by the year 2030. The urgency of the issue was demonstrated in 2011 when for only the second time in its existence, the U.N. General Assembly brought a health issue to the floor for consideration: chronic diseases. To date, most considerations of the issue have approached the topic from the vantage point that chronic diseases are a myriad of largely unconnected diseases and conditions arising in diverse tissues, organs and physiological systems. This book, Immunotoxicity, Immune Dysfunction, and Chronic Disease, deviates from

that prior model. It considers the interconnectivity of chronic diseases with both environmental insult of the immune system and subsequent immune dysfunction and inflammatory dysregulation as the underlying basis for many, if not most, chronic diseases. This change in the perception of environment-immune linkages to chronic disease is significant and has immediate implications both for the prevention of disease as well as for the development of more effective therapeutic approaches. Rather than considering environmental factors and types of reported immune alterations (e.g., depressed humoral immunity) as is common in books involving immunotoxicity, the present book approaches the environment-immune-disease triad from the standpoint of the disease. Each chapter emphasizes one or more specific immune dysfunction-based chronic disease(s) or condition(s) (e.g., asthma, atherosclerosis, multiple sclerosis, lupus) and describes: 1) the suggested environmental risk factors, 2) the underlying immune dysfunction(s) associated with the disease and 3) the overall health consequences of the disease. This book is an early entry for a new Toxicology book series for Springer titled: Molecular and Integrative Toxicology (MaIT). The series will feature detailed research information, but in the context of a more integrative or holistic framework. As part of this framework, the chapters will contain a section on "Key Points" as well as "Recommendations" where appropriate. The goal is to cover the most timely, state-of-the-art issues in toxicology as well as to ensure that the information is maximally accessible for research scientists, teachers, physicians and students. We are particularly grateful to the numerous chapter authors for providing comprehensive and expert disease-oriented contributions. We are also appreciative of their willingness to consider their material not as disparate pieces of what has become a major health crisis, but rather as key pieces in a network of apparently interconnected health challenges.

Safety pharmacology is the evaluation and study of the pharmacological effects of a potential drug that are unrelated to the desired therapeutic effect. These effects often present a hazard—particularly in individuals with compromised or limited organ system functions. *Safety Pharmacology in Pharmaceutical Development: Approval and Post Marketing Surveillance, Second Edition* covers safety pharmacology from the regulatory requirements down to the studies that must be done to justify them. Using the author's more than 30 years of direct experience, the book incorporates tricks and practical insights for making studies work and understanding why they fail. The second edition includes current regulations, including USFDA and those from Europe and Japan. Presenting a clear description of what is needed and why for supporting drug development, the book focuses on updated test methods, interpretation, and science. It covers the core and supplemental batteries of test procedures and how to do them and provides an overview of available facilities and contract organizations for performing studies.

Immunopharmacology: A New Discipline of Immense Potential Among the

looming triumphs of the biologic revolution is the rapidly developing understanding of the mechanisms of bodily defense. In the short span of 35 years, knowledge of immunologic machinery has progressed from crudest description to major understanding in cellular and molecular terms. Antibodies, immunoglobulins, and the complement system have been almost completely defined in detailed molecular terms. Organs, like thymus, spleen and lymph nodes—so long enigmatic black boxes—are beginning to be understood not only in cellular terms but in molecular, physiologic, and endocrinologic terms. With this surging new information about the immune system comes the possibility of developing a pharmacology which can modulate and control immunologic functions. Immunopharmacology most broadly conceived must address (1) control of development and function of the cellular components of the immunologic apparatus; (2) facilitation and suppression of function of the immunologically competent cells of the several subclasses, like T helpers, suppressors, and effectors, and B effectors and suppressors; (3) manipulation and repair of the major biologic amplification systems, e. g. , the complement system and kinin-kallikrein system, and (4) utilization, modulation, and inhibition of the galaxy of molecules generated by T lymphocytes, the lymphokines. This new pharmacology must deal with the fundamental effector mechanisms of immunity, namely inflammation, phagocytosis, vascular reactivity, and blood coagulation. Furthermore, immunopharmacology must address and manipulate cell-cell communication and interaction, so vital to control of the immunological apparatus.

Vichy, France, 22-24 September, 1997

Modulation and Combination Effects an Inventory of the Many Factors which Influence Carcinogenesis

Immunotoxicity, Immune Dysfunction, and Chronic Disease

8th Summer School in Immunotoxicology

Environmental Health Perspectives

Continuing the tradition set by the first and second editions, each a bestseller in its own right, the third edition of Immunotoxicology and Immunopharmacology provides reviews of environmental agents, updated to reflect the latest information on how these agents influence immune system function and health. For the first time in the book's history, an entire section covers the phylogeny and ontogeny of the immune system, spanning levels of biological complexity from earthworms to marine mammals.

History of Immunotoxicology offers the first book-length exploration of the development and importance of the field of immunotoxicology, describing the adverse health effects involving the immune system, hypersensitivity and autoimmunity. It explores new avenues of research and

immunotoxicity evaluation, regulatory aspects of immunotoxicology, and the withdrawal/banning from the market of several approved drugs and chemicals due to their immunotoxic effects. In addition, clinical manifestations of immunotoxicity, such as anaphylaxis, opportunistic infections, lymphomas, cytokine storm, and immunotherapy are addressed. Finally, the book considers how the recent past can provide insights on the future practice of immunotoxicology. As preventive measures are implemented to reduce risks, including banning of chemicals or applications of one given chemical, current toxicologists may not be aware of the toxicity potential of chemicals. This book will be of interest to students and researchers in government, industry and academia who have an interest in immunotoxicology. Examines the development of immunotoxicology Provides context to current debates on the actual toxicity potential of chemicals Covers major developments and areas of immunotoxicology

This is a review of clinical adverse effects on the human immune system that may occur following drug treatments and chemical exposures. Current and prospective models and assays that can be used to predict these adverse effects in animal toxicity studies or in human beings are described.

Prague, Czech Republic, 29 May - 2 June 1994

Toxicology of the Kidney

Immunotoxicology

Global Health Implications : January 9-11, 1994, Washington, DC

Safety Pharmacology in Pharmaceutical Development

Papers presented at the International Seminar on the Immunological System as a Target for Toxic Damage - Present Status, Open Problems and Future Perspectives

This second edition provides a synthesis of recent research on the mechanisms of chemically-induced kidney injury. The text includes a review of current concepts of clinical nephrotoxicity and renal failure, and mechanisms of specific classes of nephrotoxic drugs and environmental chemicals.

IMMUNE SYSTEM. ANTIMICROBIAL AGENTS. ANTIPARASITIC AGENTS. NERVOUS SYSTEM. CARDIOVASCULAR SYSTEM. GASTROINTESTINAL TRACT. HORMONES. HORMONE ANTAGONISTS. RESPIRATORY SYSTEM. BLOOD ANTI-INFLAMMATORY DRUGS. VITAMINS. IMMUNODEPRESSIVE DRUGS. IMMUNOENHANCING DRUGS. HEAVY METALS.

PESTICIDES. INDUSTRIAL CHEMICALS. AIR POLLUTION. FOOD. FOOD ADDITIVES. FOOD CONTAMINANTS. COCAINE. NARCOTICS. MARIJUANA. ALCOHOL. ETHANOL. SMOKING.
Nijkamp and Parnham's Principles of Immunopharmacology
Papers Presented at the Fourth Summer School in
Immunotoxicology, Aix-les-Bains, France, 18-20 October, 1995
Advances in Immunopharmacology
Selected papers from the Sixth International Conference on
Immunopharmacology
Chemical Induction of Cancer

The first comprehensive reference on immunotoxicology using analyses based on molecular effects rather than on animal models. Following an introduction to immune system pathways and toxicity mechanisms from a systemic perspective, the main part of the book surveys individual molecular mechanisms of important immunotoxicants, from PAHs to biopharmaceuticals, and from receptor-mediated toxicity to nanoparticle toxicity. Taken together, the knowledge presented here provides an up-to-date overview of this hot topic that can be directly applied to the prediction and characterization of immunotoxic effects in drugs, chemicals, and environmental contaminants.

Current Advances in Immunology presents the advances in immunology in an easy-to-use format. The book is split into 51 main areas that are further classified into sections. Where appropriate, cross-referencing to other sections is given. The text also provides a guide on how to use the book. Papers included in the book focus on a variety of topics ranging from immunoglobulins and antigens to interferons, lymphocytes, leukocytes, and macrophages as well as natural killer cells, Langerhans cells, dendritic cells, lymphoid tissue, and humoral mediators of immune responses and immunomodulators. Other papers discuss blood groups, transplantation, anti-bacterial immunity, chronic inflammation, delayed hypersensitivity, and contact sensitivity. Immunodeficiency, immune complexes, tumor immunity, immunopharmacology and immunotoxicology, and the link between nutrition and immunity are also explored. A section devoted to psychoneuroimmunology focuses on the effect of stress on graft-versus-host reaction; immunological response to stress in agoraphobia and panic attacks; and anti-beta-endorphin immunoglobulin G in humans. This book will be of interest to working scientists in the field of immunology.

Written by two experienced toxicology lecturers, Principles of Toxicology is an easy-to-read, comprehensive textbook for a first course in toxicology at the undergraduate or graduate level - filling the acute need for a well-rounded introductory text. Students will no longer need to struggle with material that is too difficult or that has too narrow a toxicological focus. Principles of Toxicology covers this broad and interdisciplinary field from the viewpoint of three different functional levels: molecular and cellular; physiological; and environmental and ecological. Within each chapter, the

authors combine background material with new information in a manner that stresses principles and concepts. These principles are then illustrated with selected specific examples. This design helps students focus on understanding the subject rather than simply memorizing details. Your search for the perfect introductory toxicology text is over! Principles of Toxicology elegantly facilitates the teaching and learning of this challenging subject.

T Lymphocytes Subpopulations in Immunotoxicology

Immunotoxicology Strategies for Pharmaceutical Safety Assessment

Current Advances in Immunology

Immunotoxicology and Immunopharmacology, Third Edition

Interactions of the Immune System with Other Systems :

Immunotoxicological Relevance : Arles, France, 14-16 September 1999

This text provides a concise and comprehensive introduction to key immunotoxicological issues for all those interested in, but with no prior knowledge of, this area of toxicology. The first section explores the health consequences of immunotoxicity, namely the adverse effects related to chemically-induced immunosuppression and immunostimulation, hypersensitivity reactions and autoimmune diseases, with an overview of major immunotoxicants. The second part describes the latest methods used to detect and evaluate, preclinically and clinically, the unexpected immunotoxic effects of xenobiotics. Trends in implementing strategies and recent changes to the regulatory aspects are also considered. The third section examines possible future developments, including In Vitro methods, biomarkers of immunotoxicity and risk assessment.

Principles of Immunopharmacology provides a unique source of essential knowledge on the immune response, its diagnosis and its modification by drugs and chemicals. The 4th edition of this internationally recognized textbook has been revised to include recent developments, but continues the established format, dealing with four related fields in single volume, thus obviating the need to refer to several different textbooks. The first section of the book, providing a basic introduction to immunology and its relevance for human disease, has been updated to accommodate new immunological concepts, particularly the role of epigenetics and the latest understanding of cancer immunology. The second section on immunodiagnosics offers a topical description of widely used molecular techniques and a new chapter on imaging techniques. This is followed by a systematic coverage of drugs affecting the immune system, including natural products. This third section contains 15 updated chapters, covering classical immunopharmacological topics such as anti-asthmatic, anti-rheumatic and immunosuppressive drugs, but also deals with antibiotics, plant-derived and dietary agents, with new chapters on monoclonal antibodies, immunotherapy in sepsis and infection, drugs for soft-tissue autoimmunity and cell therapy. The book concludes with a chapter on immunotoxicology and drug safety tests. Aids to the reader include a two-column format, glossaries of technical terms and appendix reference tables. The emphasis on illustrations is maintained from the first three editions. The book is a valuable single reference for undergraduate and graduate medical and biomedical students, postgraduate chemistry and pharmacy students, researchers in chemistry, biochemistry and the pharmaceutical industry and researchers lacking basic immunological knowledge, who want to understand the actions of drugs on the immune system.

This third thoroughly revised edition, written by a renowned expert in this rapidly expanding field, is a welcome and timely publication in the field of experimental and clinical immunotoxicology. Immunotoxicology is a young, but rapidly expanding area of toxicology. Since the second edition of this book was published in 1988, an increasing amount of data has resulted in the publication of many articles and reviews. This book covers the many general facets of current immunotoxicology - clinical, experimental, mechanistic and regulatory aspects, including a chapter on the immune system giving toxicologists unfamiliar with immunology the opportunity to acquire the minimal knowledge necessary to conduct and interpret immunotoxicity studies. A comprehensive chapter on adverse effects in relation to immunotoxicity is included in order to predict and understand the toxic effects of drugs and other chemicals in living beings. An effort is made to answer one of the perhaps most confusing issues confronting the student of immunotoxicology namely the identification of what constitutes an immunotoxic response and what does not. Researchers from different disciplines have shown interest in this field, and presented results of their work on immunotoxicological issues from extremely varied perspectives. As a bridging discipline between immunology and toxicology, immunotoxicology is genuinely multidisciplinary, reflected in this excellent book. Immunotoxicology of Drugs and Chemicals: Principles and methods of immunotoxicology Estrogens in the Environment, III

6th Summer School in Immunotoxicology

Information Resources in Toxicology

Preclinical Safety Evaluation of Immunotherapeutics, Nice, France, 23-25 October 2000

An important reference which provides an overview of the current and recently introduced methodologies for testing the immunotoxic risks in drug candidates Helps readers understand the significance of the methods and approaches to immunotoxicology testing Aids drug scientists in industry and regulatory areas to consolidate approaches to immunotoxic testing Offers a definitive assessment of nonclinical models to study the toxic impacts (bio)pharmaceuticals can have on the immune system Includes chapter authors from across the pharma industry, bringing a real-world and applied perspective to immunotoxic testing

In the approach to the analysis of disease, including, of course, cancer, two major thrusts may be distinguished. These may be referred to, in shorthand, as agents and processes: the causative agents (chemical, microbial, physical, environmental, and psychosocial) and the organismic processes, initiated and furthered by the agents, culminating in observable pathology (at the macromolecular, cytological, histological, organ function, locomotor, and behavioral levels). The past 25 years, since the appearance of the first volume of the predecessor series (1) authored by the Editors of this present volume, have seen an impressive number of studies on chemicals (and other

agents) as etiologic factors in the induction of cancer. The major emphasis has been on the discovery of many chemical carcinogens of widely different structures, their metabolism by various tissues and cells, and, in turn, their molecular-biochemical effects on the cells. This rapidly expanded body of information, as effectively covered in the predecessor volumes, is an excellent entree to the second half of the overall problem of chemical carcinogenesis, the processes. The active agents trigger a large array of molecular-biochemical alterations to which the target cells, target tissues, and target organisms respond in many select and common ways. This second major aspect of the induction of cancer by chemicals (and by other agents)- the sequence of cellular and tissue changes clearly relevant to cancer-remains the challenge for the future. The rapid developments in immunology in recent immunomodulatory drugs can be distinguished years have dramatically expanded our knowledge of from their beneficial therapeutic effects. mammalian host defence mechanisms. The molecu- Currently, it is only possible to obtain an overview lar mechanisms of cellular interactions during of these various aspects of immunopharmacology immune responses have been unravelled, the intra- by reading a range of immunological, pharmacol- cellular responses involved in signal transduction ical, diagnostic and toxicological literature. Good delineated and an ever-increasing number of soluble immunological textbooks are available, while mediators of immune and inflammatory reponses immunopharmacology is covered mainly in terms of have been discovered. the inflammatory response. Principles of Immuno- The initial result of this explosion of knowledge pharmacology is intended to provide for the first time has been to provide the researcher and the clinician in a single volume a basic understanding of with an arsenal of diagnostic tools with which the immunological mechanisms, a review of important immunological bases of disease processes can be immunodiagnostic tools and a description of the investigated. This has made disease diagnosis much main pharmacological agents which modify the more precise, enabling the physician to tailor therapy immune response, together with an introduction to much more closely to the individual patient's needs. immunotoxicology. As such we hope that it will be However, better understanding of disease processes useful as a reference text for physicians, researchers only provides a

gradual improvement in therapy. This and students with a rudimentary knowledge of is because the new molecular targets that have been immunology.

Principles of Immunopharmacology

Principles and Methods of Immunotoxicology

Approval and Post Marketing Surveillance, Second Edition

7th Summer School in Immunotoxicology

9th Summer School in Immunotoxicology

T Lymphocyte Subpopulations in Immunotoxicology Edited by Ian Kimber ZENECA Pharmaceuticals, Central Toxicology Laboratory, Macclesfield, Cheshire, UK and Mary Jane K. Selgrade US Environmental Protection Agency, National Health and Environmental Effects Research Laboratory, NC, USA Immunotoxicology is a diverse discipline that embraces the investigation of the adverse health effects that may result from the interaction of xenobiotics with the immune system. T lymphocytes orchestrate adaptive immune responses and are of central importance in the consideration of immunotoxicity. These cells and/or the tissue responsible for their functional maturation (the thymus) have been implicated as the primary or secondary targets for chemical insult. Moreover, T lymphocytes play pivotal roles in the induction and elicitation of chemical and protein allergy and in the pathogenesis of autoimmune disease. Classically, T lymphocytes have been divided into two main populations: CD4 helper T cells and CD8 suppressor/cytotoxic T cells. It is now apparent that there exists within both populations considerable functional heterogeneity, characterized usually by variable cytokine secretion patterns. Two major subpopulations of T helper (Th) cells have been identified and designated Th1 and Th2, with similar, but less well characterized, sub-types of cytotoxic (Tc) cells having been described also. The discovery of functional subpopulations of Th (and Tc) cells has profoundly influenced our view of the immune response and, in particular, our appreciation of the way in which the immune system can tailor responses to meet challenges of different types. This has also translated into a much more detailed understanding of certain immunopathologic processes and the role of T lymphocytes in the development of allergic, autoimmune and inflammatory diseases. This book explores the role of T lymphocyte subpopulations in the development and expression of immunotoxic effects. Constituent chapters reveal that a consideration of the impact of chemicals on these diverse T cell populations and the polarization of T cell responses has already contributed greatly to our understanding of the mechanisms underlying immunotoxicity, including immune suppression and allergic and autoimmune responses. Now in its revised and updated Second Edition, this volume is the most comprehensive and authoritative text in the rapidly evolving field of environmental toxicology. The book provides the objective information that health professionals need to prevent environmental health problems, plan for emergencies, and evaluate toxic exposures in patients. Coverage includes

safety, regulatory, and legal issues; clinical toxicology of specific organ systems; emergency medical response to hazardous materials releases; and hazards of specific industries and locations. Nearly half of the book examines all known toxins and environmental health hazards. A Brandon-Hill recommended title.

Immunotoxicology of Drugs and Chemicals

Proceedings of the First International Conference on Immunopharmacology,
July 1980, Brighton, England

Immunotoxicity

Molecular Immunotoxicology

Principles of Toxicology