

Book review: *Safety of Biologics Therapy*

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Safety of Biologics Therapy: Monoclonal Antibodies, Cytokines, Fusion Proteins, Hormones, Enzymes, Coagulation Proteins, Vaccines, Botulinum Toxins (Cham, Switzerland: Springer International Publishing; 2016) by Brian A Baldo from the Molecular Immunology Unit, Kolling Institute of Medical Research, Royal North Shore Hospital of Sydney, and the Department of Medicine, University of Sydney, Australia, is a book that belongs on the shelf of everyone in the field of biologic therapies research and clinical practice. In writing this book, the author's intention was to produce an up-to-date text book on approved biologic therapies, as far as that is possible in this time of rapidly evolving developments in biotherapeutic research and the introduction of new and novel agents for clinical use.

The monograph comprises 610 pages in 13 chapters, each including a summary and further reading suggestions. All chapters include a discussion of basic and clinical material. Well-designed, comprehensive tables and color figures are present throughout the book. The book itself examines the biologic products that have regulatory approval in the USA and/or European Union and that show every indication of remaining important therapies. It covers in great detail all the latest work on peptide hormones and enzymes, monoclonal antibodies, fusion proteins, and cytokine therapies. Beyond that, it also presents the latest information on blood coagulation proteins, vaccines, botulinum neurotoxins, and biosimilars.

A unique aspect of this book is that it is the first academic text that to make such a detailed study of approved biologic therapies in an era of ongoing research and development in this field with its flourishing new knowledge. Starting with the first biologic recombinant product, human insulin (Humulin®, Eli Lilly and Company, Indianapolis, IN, USA), approved in 1982, currently more than 200 biologic drugs are on the market. It is predicted that by 2016, biological drugs will make up half of the world's 20 top-selling drugs, and by 2018, the sales of these agents will account for almost half of the world's 100 biggest sellers. The first chapter of the book considers how biologic agents are to be classified and assessed for characterization, manufacturing, and control; product development; identity; purity; and potency. The first chapter reviews adverse reactions to the drugs and provides definitions and a classification of such adverse reactions, including those that may be associated with

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biologic therapies. The syndromes associated with biologic therapies, such as capillary leak syndrome, cytokine release syndrome, hemophagocytic lymphohistiocytosis, macrophage activation syndrome, and tumor lysis syndrome are well defined and characterized. Other rare complications of biologic therapies such as systemic inflammatory response syndrome, posterior reversible encephalopathy syndrome, and immune reconstitution inflammatory syndrome are also described.

The subsequent three chapters include a discussion of the basic and clinical aspects of therapeutic monoclonal antibodies approved for cancer therapy. These chapters are perhaps the most important in the book, at least from a clinical standpoint. Within these chapters, the author considers technological advances in the production of monoclonal antibodies, their nomenclature, the approved indications for the currently approved monoclonal antibodies and antibody–drug conjugates, as well as the range of side effects and future prospects of monoclonal antibody therapy.

The next chapter includes a discussion of cytokines, including interferons, colony-stimulating factors (CSFs), and epoetin alfa (rhEPO). The author examines the known and potential toxicities of cytokines and indicates that the presence of adverse effects does not negate the clear clinical improvements offered by approved cytokines. Of the more than 130 currently known cytokine products populating the Center for Drug Evaluation and Research-approved Biologic Products list, only 23 are approved for use by the US Food and Drug Administration (FDA), with all 23 being manufactured by recombinant DNA technology. The chapter also reviews the properties of alfa, beta, and gamma interferons. As it is important for the clinician to know that virtually all patients treated with interferons experience some adverse effects at some time during therapy, all of these are well covered in the chapter. The exhaustive descriptions include an extensive range of adverse reactions including cardiovascular, respiratory, endocrine, hematologic, metabolic, urinary tract, and skin adverse events, as well as adverse effects on the nervous and sensory systems. The author also presents a long list of adverse reactions provoked by CSFs, with the most commonly occurring headache, bone pain, myalgia, fever, flushing, and cutaneous reactions being described in detail. In addition, the chapter also examines the significant but rarely observed adverse effects of rhEPO, including the serious reactions observed in anemic patients with end-stage renal disease, including myalgias, iron deficiency, elevated blood pressure, and seizures. Importantly, erythropoietin receptors have been demonstrated in tumor tissue, and the

cytokine itself may support tumor angiogenesis, suggesting the possibility that erythropoietin may initiate tumor growth or aid tumor progression.

The following chapter moves to the topic of fusion proteins, produced by genetic engineering. This process produces a new polypeptide by the incorporation of separate domains, with the new protein possessing the functional properties of the component proteins. There are currently eleven approved chimeric fusion proteins on the market, and many more are at different stages of clinical development. The most commercially successful fusion protein is etanercept, but other agents from this group of biological drugs including romiplostim and factor VIII Fc fusion protein are enjoying greater success. Clotting factor fusion proteins are discussed in detail in Chapter 10, and these are with regard to blood coagulation. Together with other potential treatment complications, the chapter also discusses the nature of immediate and delayed occurrence of hypersensitivity to fusion proteins, the most common side effect to their use.

The subsequent two chapters discuss peptide hormones and glycoprotein hormones. The examined peptide hormones include insulin, human growth hormone, synthetic analogs of somatostatin, glucagon, vasopressin, and oxytocin. Adrenocorticotrophic hormone (also known as corticotropin), gonadotropin-releasing hormone, and parathyroid hormone are also included. The structure of these agents is highly heterogeneous. They may be small peptides, such as oxytocin and vasopressin, each of which with only nine amino acids, or somewhat larger, such as insulin with 51 and growth hormone with 191 amino acids. Of the glycoprotein hormones, follicle-stimulating hormone, luteinizing hormone, human chorionic gonadotropin, and thyroid-stimulating hormone are examined. The book also goes on to review the enzymes approved for replacement therapy of Gaucher disease and lysosomal storage diseases.

The final three chapters cover vaccines, botulinum neurotoxins, and biosimilars. The final chapter, examining biosimilars, is particularly important. They are defined as agents that meet the extremely high standards for comparability or similarity to the original biologic drugs and they are approved for use in the same indications. The key value of biosimilars is that they are high-quality drugs that possess similar properties to their original counterparts, but at a lower cost that makes them available for a wider population of patients.

In summary, *Safety of Biologics Therapy: Monoclonal Antibodies, Cytokines, Fusion Proteins, Hormones, Enzymes, Coagulation Proteins, Vaccines, Botulinum Tox-*

ins by Brian A. Baldo is an informative and easily readable book. It will be helpful for students, fellows, clinicians, and researchers who wish to improve their knowledge of the biology, pharmacological efficacy, and safety of biological drugs.

Disclosure

The author reports no conflicts of interest. This editorial represents the opinions of the authors, and has not been reviewed or prepared as part of any government agency or companies listed.

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