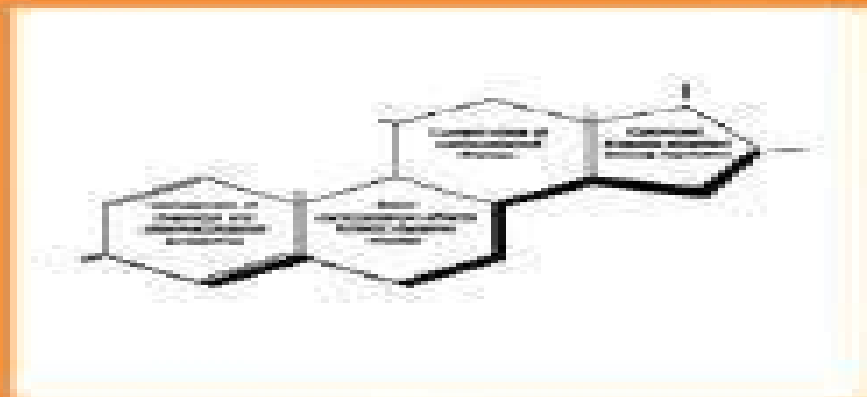


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# Glucocorticoid Therapy in Chronic Inflammatory Bowel Disease

From Basic Principles to  
Rational Therapy



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# Glucocorticoid Therapy In Chronic Inflammatory Bowel Disease From Basic Principles To Rational Therapy

**H.W. Mollmann, B. May**



## **Glucocorticoid Therapy In Chronic Inflammatory Bowel Disease From Basic Principles To Rational Therapy:**

**Glucocorticoid Therapy in Chronic Inflammatory Bowel Disease** H.W. Mollmann, B. May, 1996-10-31 The clinical efficacy of glucocorticoids in the treatment of inflammatory bowel disease has been confirmed in a multitude of controlled monocentre and multicentre studies as well as from observations of the clinical course of the disease Although in the past the treatment recommendations dose regimen substance selection and mode of administration were deduced principally from clinical trials in recent years experimental research has yielded a mass of therapeutically significant new results This seeks to optimize the clinical effects of the steroids and minimize their adverse events on a rational basis by the application of the knowledge obtained in pharmacokinetic and pharmacodynamic models taking into account the different types of protein binding and the intrinsic activity of the various glucocorticoids However the transfer of this type of disease adapted differential glucocorticoid treatment into a clinical context involves a critical examination of the received notions that have characterized steroid treatment in the past such as strictly circadian administration or time related dose reduction as well as proof of the clinical superiority of the new therapeutic approaches This book the proceedings of a workshop on Glucocorticoid Treatment held in Strasbourg France identifies the current status of existing therapeutic concepts in inflammatory bowel disease presents the pharmacokinetic and pharmacodynamic interactions in connection with the specific pharmacological properties of steroids with reference to substance differences and different modes of administration and demonstrates their therapeutic significance Inflammatory Bowel Disease: Translation from Basic Research to Clinical Practice B. Vucelic, J.F. Colombel, C. Gasche, J. Schölmerich, 2004-12-09 The amount of information on the pathogenesis of inflammatory bowel disease is growing rapidly This is reflected by a continuous increase in the number of papers presented at international GI meetings To make things more difficult for practicing physicians there is also a large number of new clinical trials being published which require periodical critical reviews and recommendations Faced with these issues the scientific committee of the Falk Symposium No 140 decided to take a different approach and to apply a novel format that is reflected in the title of the Symposium Translation from basic research to clinical practice This book contains the proceedings of that Symposium held in Dubrovnik Croatia on May 7 8 2004 The sections are designed so that they start with the information from basic sciences on different aspects of these complex diseases and further lead to their clinical implications Special attention is paid to the mechanisms of actions of established drugs The last two sections are clinically oriented and focus on the most difficult aspects of both Crohn s disease and ulcerative colitis This format provides state of the art chapters by leading experts in the field and at the same time up to date information on the clinical application of the new knowledge Immunosuppression in Inflammatory Bowel Diseases K. Fellermann, D.P. Jewell, W.J. Sandborn, J. Schölmerich, E.-F. Stange, 2001-06-30 The aetiology of the chronic inflammatory bowel diseases Crohn s disease and ulcerative colitis is still enigmatic The therapeutic approach has therefore traditionally focused on anti inflammatory

principles including corticosteroids and aminosalicylates Since a significant proportion of patients is steroid dependent or refractory and because of the problematic side effects of long term systemic steroids active immunosuppression has gained acceptance in the field The classical immunosuppressants azathioprine and 6 mercaptopurine have long been evidence based in IBD but underused Recently methotrexate and cyclosporine have also been proven to be effective in certain situations Newer drugs like tacrolimus mycophenolate and others may be similarly useful but their potential is still unclear Finally the immune modifiers including IL 10 and TNF antibodies have been successfully subjected to controlled trials Other experimental drugs discussed in this book are on the horizon This volume is the Proceedings of Falk Symposium 119 held in Freiburg im Breisgau Germany October 3 4 2000 and covers systematically the field of immunosuppression in inflammatory bowel diseases It is hoped that it will further the prudent use of these drugs in the proper clinical situations by increasing our understanding of both the mechanisms of action and the clinical benefit to the patient

*VI International Symposium on Inflammatory Bowel Diseases* D. Rachmilewitz, R. Modigliani, D.K. Podolsky, D.B. Sachar, N. Tozun, 2002-06-30 This book the proceedings of Falk Symposium No 123 VI International Symposium on Inflammatory Bowel Diseases held in Istanbul Turkey on September 3 5 2001 focuses on the issues and controversies pertinent to IBD in the 21st century The achievements in medical surgical and in the basic sciences in the last twenty years since the first Jerusalem IBD Symposium are summarized in detail Controversies with respect to the medical treatment of inflammatory bowel diseases are discussed One section deals with surgical issues such as laparoscopic surgery in inflammatory bowel diseases ileo anal pouches and the surgical treatment of Crohn s disease The last section is devoted to the biological treatment of IBD and to the needs both in medical science and in the clinic

Advances in Inflammatory Bowel Diseases P. Rutgeerts, J-F. Colombel, S.B. Hanauer, J. Schölmerich, Guido Tytgat, A. van Gossum, 1998-12-31 Ulcerative colitis and Crohn s disease remain a great therapeutic challenge to the medical community In recent years knowledge about the pathogenesis of these diseases has progressed rapidly but the cause of the diseases remains completely unknown It has become clear that dysregulation of the mucosal immune system is the basis for the chronic evolution of the diseases in a genetically susceptible population Exciting new therapeutic approaches have been attempted in the last couple of years and cytokine and anti cytokine treatments in particular seem very promising especially in intractable disease The format of the Falk Symposium 106 on Advances in Inflammatory Bowel Diseases held in Brussels Belgium June 18 20 1998 was somewhat innovative as each session attempted to link the new insights into pathogenetic mechanisms with new therapeutic approaches resulting in optimal information transfer The classic therapeutic schemes were updated with a special focus on step wise build up of therapy

**Mechanisms of Intestinal Inflammation** R. Duchmann, 2004-04-30 In recent years considerable progress has been achieved in regard to our understanding of the induction and modulation of the immune response in the intestinal mucosa It is clear that this mucosal immune reaction is predominantly steered by certain T cell populations which are characterized by

their cytokine secretion profile Less well known are the conditions under which the uptake and processing of a specific antigen leads to a certain immune response whether it be protective tolerant or inflammatory However here again distinct progress has been made in our understanding Equally significant for immune regulation in the gut appears to be so called innate immunity Every shift of equilibrium in the highly regulated mucosal immune reaction is accompanied by an inflammatory reaction and destruction of the mucosa In nearly all cases this inflammatory response is dependent on the presence of bacterial intestinal flora This book the proceedings of Falk Symposium 133 on Mechanisms of Intestinal Inflammation Implications for Therapeutic Intervention in IBD held in Berlin Germany on 10 11 June 2003 summarizes present knowledge in the area of unspecific and specific immune reactions in the gut recording the gaps in our knowledge and in particular presenting the possibilities of targeted intervention The link to inflammatory bowel diseases Crohn s disease and ulcerative colitis is always in focus Chapters by an international panel of basic scientists clinical researchers and clinicians also record the problems which can originate through today s possible modulation of the immune reaction setting the basis for review of clinical problems This book is valuable readings for all scientists and physicians who from different perspectives have an interest in research on IBD and in the clinical management of these diseases **Glucocorticoid**

**Therapy in Chronic Inflammatory Bowel Disease** H. W. Möllmann, B. May, 1996 **Topical Steroids in Gastroenterology and Hepatology** A. Dignass, V. Gross, H.J. Buhr, O.F.W. James, 2004-02-29 This book the proceedings of a Falk Workshop on Topical Steroids in Gastroenterology and Hepatology held in Berlin Germany on 14 June 2003 critically discusses the current role of budesonide in gastroenterology hepatology surgery and oncology and focuses especially on potential new indications for the use of budesonide A number of smaller clinical studies and anecdotal case reports with impressive clinical effects are reported in patients with gastrointestinal hepatic oncological and surgical problems In addition the use of budesonide for the treatment of distal ulcerative colitis and ileocolonic Crohn s disease is evaluated with respect to its role in an evidence based management of IBD Finally as clinical experience with the use of budesonide is increasing safety issues and the side effect profile of budesonide is addressed **Induction and Modulation of Gastrointestinal**

**Inflammation** A. Stallmach, M. Zeitz, W. Strober, Thomas MacDonald, H. Lochs, 1998-12-31 This book the proceedings of Falk Symposium No 104 organized in collaboration with the Society of Mucosal Immunology and held in Saarbrücken Germany March 5 7 1998 is centered around the immunological mechanisms of mucosal protection and their disturbances leading to intestinal inflammation and destruction This is a rapidly expanding field involving recent knowledge of basic immunology and cell biology as well as clinical observations The conference and this book summarize very recent data in this field and suggest strategies for future research and clinical applications and will be of interest to both basic scientists and clinicians

*Prevention of Progression in Chronic Liver Disease* N. Hiyashi, M.P. Manns, Marianne Manns, Nariyuki Hayashi, 2004-07-21 In several liver diseases the underlying cause cannot always be eliminated i.e. the progression of liver

disease cannot be prevented This is particularly true for non responders to the treatment of chronic hepatitis C HCV It is relevant for more than 40% of patients with HCV genotype 1 and up to 20% of patients with genotype 2 or 3 Several approaches are now underway to prevent or ameliorate mechanisms of disease progression In Asia and particularly in Japan Glycyrrhizine SNMC has been widely used for this purpose At present SNMC is under clinical evaluation in Europe This book the proceedings of the Falk Workshop on Prevention of Progression in Chronic Liver Disease An Update on SNMC Stronger Neo Minophagen C Part IV of the XII Falk Liver Week in honour of Hans Popper s 100th birthday held in Freiburg Germany on 22 October 2003 is devoted to the understanding of basic mechanisms of fibrogenesis the state of the art of non invasive markers of disease progression that may substitute liver biopsy in the future and of other predictive parameters indicating disease progression in particular the development of hepatocellular carcinoma All these problems are particularly relevant for chronic hepatitis C A better characterization of so called non responders for the treatments available is crucial for the development of new strategies preventing or postponing disease progression Such strategies should influence fibrogenesis and thus cirrhosis formation as well as the development of life threatening complications of liver cirrhosis including hepatocellular carcinoma In this volume the available information on SNMC as an approach to prevent progression of chronic liver disease is discussed by several internationally renowned authors who report on the mechanisms of liver fibrogenesis and fibrolysis on non invasive markers of disease progression and on hepatocellular carcinoma as one of the major complications of liver cirrhosis nowadays Finally experts from Japan report on their knowledge and experience concerning the drug SNMC Glycyrrhizine in the prevention of cirrhosis and HCC and first study results from Europe are presented

Malignant Liver Tumours: Basic Concepts and Clinical Management F. Berr,J. Bruix,J. Hauss,Ch. Wittekind,J.

Wands,2002-11-30 Hepatocellular carcinoma HCC and cholangiocarcinoma CC both increasing in incidence have become a major topic of basic and clinical research as well as clinical practice in hepatology Experts in the field update the current concepts on the carcinogenesis of HCC and CC such as genetic alterations in the pathways of cell cycle and apoptosis regulation the hypothesis of dedifferentiation of hepatocytes to the malignant phenotype vs that of activation of hepatic progenitor cells incapable of maturation maturation arrest hypothesis In spite of an increasing number of genetic alterations described in human HCC as well as cell regulatory pathways tested in experimental HCC models the key hits causing progression of the cell cycle in imbalance with apoptosis tissue invasive growth and metastatic potential of cell clones still remain elusive Very powerful genomic and proteomic techniques are promising insights into the carcinogenesis of liver malignancies that will allow more efficient therapeutic strategies The current concepts on risk profiling surveillance of risk groups and therapeutic strategies are evidence based for HCC and less detailed for CC Surveillance of risk groups improves detection of liver tumours in curable stages Best strategies for curative treatment of HCC use neoadjuvant antitumour therapies before liver transplantation and a role is emerging for living donor related liver transplantation New palliative

therapies for HCC are in the experimental stage with biological response modifiers including angiogenesis inhibitors and entering phase II clinical trials with the alpha fetoprotein derived vaccines

*Biology of Bile Acids in Health and Disease* G.P. van Berge Henegouwen, D. Keppler, U. Leuschner, G. Paumgartner, A. Stiehl, 2001-05-31 Beginning in 1970 the International Bile Acid Meeting has taken place every two years and each time new progress in our understanding of the complex role of bile acids in many metabolic processes of the liver and the intestine has been revealed by a selected group of leading scientists from all over the world Although originally mainly physiological data on bile acid synthesis and transport were emphasized and later on also the therapeutic benefit of bile acids in gallstone disease and cholestasis was discovered we have come now to the molecular biology and genetic era with major discoveries in transport defects and related diseases This book is the proceedings of Falk Symposium No 120 held in The Hague The Netherlands on October 12 13 2000 the 16th International Bile Acid Meeting One of the main discoveries recently has been the identification of nuclear receptors for bile acids which gives them a much broader perspective than previously anticipated It even suggests that bile acids can regulate their biosynthesis and enterohepatic circulation transcriptionally It will therefore not be surprising that this topic together with the molecular regulation of cholesterol 7 $\alpha$  hydroxylase and cholesterol homeostasis has a dominant place in these proceedings Another important topic is the progress in our molecular understanding of hepatic both at the basolateral and canalicular sites cholangiocytic and intestinal bile acid transport processes Further insights into genetic defects causing cholestasis or intestinal malabsorption in animal models and in human diseases are also discussed by a number of well known authors Finally the last section deals with new findings on the role of bile acid therapy in cholestatic syndromes or chemoprevention and with the potential benefit of bile acid inhibitors All contributors provide an update on the most recent developments in their field

Bile Acid Biology and its Therapeutic Implications G. Paumgartner, D. Keppler, U. Leuschner, A. Stiehl, 2005-03-02 This book is the proceedings of the 18th International Bile Acid Meeting held as the Falk Symposium 141 in Stockholm Sweden on June 18 19 2004 The International Bile Acid Meetings have become some of the most important meetings in the bile acid field worldwide since Herbert Falk decided to sponsor these Symposia in biannual sequence in 1970 The 17 International Bile Acid Meetings in the past have been a great stimulus for new ideas and methods as well as the development of therapeutic applications of bile acids They have always been a forum where basic scientists and clinicians interact Many novel results of bile acid research were first presented at these meetings The meeting in Stockholm again attracted a large number of basic and clinical scientists interested in bile acid and biliary research from all over the world Knowledge about the regulation of bile acid synthesis bile acid transport and enterohepatic circulation in health and in disease has increased considerably during recent years Accordingly bile acid research is alive as ever A new chapter of bile acid research was opened by the finding that bile acids are ligands of nuclear receptors which regulate synthesis metabolism and transport of bile acids and steroids A large part of the book is devoted to these topics The 18th International Bile Acid

Meeting was again a truly interdisciplinary symposium at the highest scientific level Its participants enjoyed hearing the latest reports on bile acid research in the city where so many seminal studies on bile acids were performed It is hoped that the readers of this book will share the enjoyment

Intestinal Mucosa and Its Diseases - Pathophysiology and Clinics W. Domschke, R. Stoll, T.A. Brasitus, M.F. Kagnoff, 1999-07-31 These proceedings of Falk Symposium 110 on Intestinal Mucosa and its Diseases Pathophysiology and Clinics held at Titisee Black Forest Germany 16 17 October 1998 comprehensively review salient clinical as well as scientific aspects pending or settled of the main intestinal diseases In particular chapters deal with infectious and neuroendocrine diarrhoeas coeliac sprue allergic enteropathy intestinal lymphomas colorectal carcinomas and chronic inflammatory bowel diseases in terms of clinical presentation as well as underlying mechanisms This book therefore aims to bridge the gaps between basic science and clinics for the eventual treatment of patients afflicted with these diseases

**Cholestatic Liver Diseases: Therapeutic Options and Perspectives** U. Leuschner, U. Broomé, A. Stiehl, 2004-06-30 During the last decade knowledge about cholestatic liver disease and concomitant diseases such as ulcerative colitis cholangio and hepatocellular carcinoma pancreas and colon cancer has increased considerably Studies on ursodeoxycholic acid treatment alone or in combination with immunosuppressive compounds and their positive effects on biliary liver disease as well as on so called overlap syndromes or intestinal tumors are published in increasing numbers and stimulate discussion on whether or not ursodeoxycholic acid is able to improve the general condition and or life expectancy of patients On the other hand genetics aetiological and pathogenetic aspects are still difficult to comprehend but are the absolute prerequisite for the development of better treatment options This book is the proceedings of Falk Symposium No 136 Part I of the XII Falk Liver Week held in Freiburg Germany on October 15 16 2003 and contains stimulating exciting and controversial papers on clinical and also basic research at the highest scientific level

*The Gut as a Model in Cell and Molecular Biology* F. Halter, D. Winton, N.A. Wright, 1997-12-31 There are many separate groups working in gut biology and they feel that the gut is an excellent model for investigating general problems in differentiation growth control stem cell biology and regeneration and adaptive responses There is a pressing need to define the objectives of the next 5 to 10 years and the meeting Part III of the Gastroenterology Symposia Freiburg 1996 Falk Symposium No 94 held in Freiburg Germany October 25 26 brought together some of these groups with a view to identifying areas which are not being utilized and need to be exploited such as transgenic and knockout approaches retrovirus delivery systems and model cell tissue systems The main themes of the book are gastrointestinal development and differentiation gut stem cell biology and the control of gut growth in normal and abnormal situations Basic research findings are related to clinical situations and the book will appeal not only to gut cell and molecular biologists but also to gastroenterologists interested in the potential applications of these subject areas

*Functional Dyspepsia and Irritable Bowel Syndrome* H. Goebell, G. Holtmann, N.J. Talley, 1998-03-31 In recent years functional gastrointestinal disorders have attracted much interest These disorders are extremely common They



are characterized by symptoms and the lack of structural lesions that can be identified with clinically available routine diagnostic tests Several functional abnormalities are now believed to play a role in the development of the symptoms This book summarizes the presentations at the International Falk Symposium No 99 Functional Dyspepsia and Irritable Bowel Syndrome Concepts and Controversies that took place on May 27 28 1997 This symposium brought together clinical and basic researchers and clinicians to improve interdisciplinary communication The meeting comprehensively covered basic and clinical aspects of these disorders and it not only summarized the current knowledge but also identified scientific questions that need to be addressed in the future

*Immunology and Liver* M.P. Manns, Marianne Manns, G. Paumgartner, U. Leuschner, 2000-08-31 In 1992 the Falk Symposium No 70 dealt with the topic Immunology and Liver At that time basic mechanisms of immunology as well as immunopathogenetic mechanisms in viral and autoimmune liver diseases were discussed Now 7 years later the Falk Symposium No 114 held in Basel Switzerland October 20 21 1999 Part I of the Basel Liver Week 1999 focused on immunology in autoimmune liver diseases In the first section basic mechanisms of autoimmunity are presented including the relevance of superantigens and the role of apoptosis A further topic is the latest developments concerning animal models for autoimmune diseases Recently the International Autoimmune Hepatitis Group newly defined and reclassified the syndrome of autoimmune hepatitis Autoimmune hepatitis is now identified and studied in all parts of the world including Asia and South America A special variant of autoimmune hepatitis was identified as one organ manifestation of the autoimmune polyendocrine syndrome type 1 a genetic disease caused by mutations in a single transcription factor Drug and hepatitis virus induced immune mediated liver diseases may serve as models for nonhepatic immune mediated disorders DNA technology has increased our knowledge of the immunogenetic background of autoimmune liver diseases Among the cholestatic immune mediated liver diseases significant progress has been made concerning primary biliary cirrhosis in particular regarding the identification of mitochondrial antigens and the characterisation of the immune reactions directed at them The involvement of infectious agents in PBC as well as the definition of overlap syndromes is a particular focus for basic and clinical research in this area Concerning the therapy of autoimmune liver diseases corticosteroids and azathioprin remain the state of the art for autoimmune hepatitis while bile acids have become well established in treatment of primary biliary cirrhosis as well as primary sclerosing cholangitis New drugs in the future will include topical steroids such as budesonide and new immunosuppressive agents like mofetil mycophenolate Liver transplantation is the treatment of choice for end stage liver diseases all autoimmune liver diseases are among the best candidates for liver transplantation Hopefully new therapeutic strategies based on the results obtained from experimental models will become everyday clinical practice in the next decade Therefore this symposium concludes with a discussion

**Immunological Diseases of Liver and Gut** M. Lukás, M.P. Manns, J. Spicak, E.-F. Stange, 2004-06-30 This book is the proceedings of the Falk Symposium No 135 held in Prague Czech Republic on September 12 13 2003 and is dedicated to the

important issue of immunological aspects of diseases of the liver and gut Without any doubt immunological pathways are among the most important and universal factors in the pathogenesis of all diseases Their importance is also constantly increasing because these principles have been adopted in clinical practice for both diagnostic and therapeutic procedures Chapters by prominent experts will stimulate new ideas and set the scene for productive discussion on this topic

*Cytokines in Liver Injury and Repair* A.M. Gressner, P.C. Heinrich, S. Matern, 2002-06-30 This book the proceedings of Falk Symposium No 125 on Cytokines in Liver Injury and Repair Progress in Gastroenterology and Hepatology Part II held in Hannover Germany on September 30 October 1 2001 provides an update of our current knowledge on the role of cytokines in various human and experimental liver diseases and on their present and prospective use in therapeutic trials The book contains chapters by most well known experts in the field who have contributed significantly to our present knowledge on cytokines in liver injury and repair

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