Kuntz / Kuntz † · Hepatology, Textbook and Atlas

# HEPATOLOGY

# TEXTBOOK AND ATLAS

History · Morphology Biochemistry · Diagnostics Clinic · Therapy

With 530 Coloured Illustrations and 321 Coloured Tables



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### **Dedication**

In 1978, my son and I began with the planning and preparation of a joint textbook on hepatology. In 1997, one year before completion of this work, Hans-Dieter died of a malignant disease. It was his wish that I should realize our mutual aim.

I have dedicated the **German edition** of the book "Praktische Hepatologie" (1998) to:

#### my unforgettable son Hans-Dieter

whose knowledge and manual skill I have always admired, whose critical as well as creative ideas for our joint book were so valuable,

who did not live to see the completion of this work as a co-author

dedicated in love and gratitude

#### **Dedications**

The 1<sup>st</sup> **English edition** of the book "Hepatology · Principles and Practice" (2002) is dedicated – also at my son's request – to:

Dr. med. Dr. rer. nat. *Herbert Falk* (Freiburg) the most generous patron of hepatological research and further education, the initiator of worldwide, international hepatology *dedicated in admiration and friendship* 

The 2<sup>nd</sup> **English edition** of the book "Hepatology · Principles and Practice" (2006) is dedicated to:

Prof. Dr. med. Heribert Thaler (Vienna)
who has united the histopathologic and clinical aspects
of hepatology in such an excellent manner,
from whom I have learned so much in many years of friendship
dedicated in esteem and cordiality

The 3<sup>rd</sup> **English edition** of the book "Hepatology · Textbook and Atlas" (2008) is dedicated to:

Prof. Dr. med. Dr. h.c. mult. *Hubert E. Blum* (Freiburg) who has enriched hepatology as a scientist, teacher and clinician in such an exemplary manner, he remains a physician with a strong sense of vocation *dedicated in appreciation and respect* 

#### **Authors**



#### Prof. Dr. med. Dr. med. h. c. Erwin Kuntz

The author spent the first 16 years of his clinical career at the Medical University Hospital in Giessen (6 years as senior physician). Then followed 20 years as head physician at the Internal Department of the Academic Hospital in Schwäbisch Hall and at the Internal Department of the Academic Hospital in Wetzlar. For 45 years, he has taken an active part in the postgraduate education of physicians; he has been an organizer of numerous scientific congresses. Erwin Kuntz has received more than 25 international awards national and honorary memberships. He has been presented the Honorary Doctorate of the University of Debrecen (Hungary) and is an Honorary Citizen of the region of Waldsolms. He is holder of the "Great Merit Cross of the Federal Republic of Germany", the "Great Merit Cross of the Republic of Italy" and the "Paracelsus Medal", which is the highest award given by the medical profession in Germany.



#### Prof. Dr. med. Hans-Dieter Kuntz

The co-author was certified as a specialist in internal medicine at the Academic Hospital in Duisburg. In 1980, he obtained his qualification as a gastroenterologist and became senior physician at the Department of Gastroenterology/Hepatology of the University Hospital in Bochum. As from 1989, he was head physician at the Department of Internal Medicine and Gastroenterology at Augusta Academic Hospital in Bochum. His many activities included the postgraduate education of physicians for 17 years. He was granted honorary membership of the Society of Gastroenterology of Uruguay (1993) and became a Fellow of the European Board of Gastroenterology (EUMS) (1996). Before the introduction of the German textbook "Praktische Hepatologie" (1998) together with his father he died due to a malignant disease at the age of 48.

#### Preface to the third Edition

Like the first edition, the second edition was sold out within one year, as was a special reprint available exclusively in the Far East. The extremely positive response from different countries around the world made it easy for both publisher and author to consider a third edition in the near future. We wished to create a textbook with an integrated hepatological atlas based on a form, colour design and scope that had not existed before. Nevertheless, we decided to keep the tried and tested concept of the original version: to serve as a teaching manual, textbook and reference work. Like its predecessor, the new edition has 40 self-contained chapters, each with its own detailed list of contents (using up to three decimal points). Once again, a big black dot is inserted whenever the following sentence represents a semantic leap from the preceding statement. The same fonts and letter sizes have been used. Each chapter finishes with an extensive bibliography. All authors are listed in full in semi-bold type and ordered alphabetically. About 7,000 references have been cited. I have retained historical papers which appeared to me to be in some way remarkable, but literature up to 2008 has also been included.

Due to the updating of the individual chapters, a revised index was required with about 3,000 terms and 12,000 page references. Using this index and the detailed table of contents at the beginning of each chapter, the reader is able to find everything easily and quickly. Furthermore, in the text itself, there are numerous cross-references to related descriptions, figures and tables in other chapters. This makes it possible to interconnect the extensive information contained in the 935-page textbook like a network.

There are more citations of first-time authors (with year) regarding syndromes, diagnostic methods, therapeutic measures, medicotechnical developments, surgical procedures, etc. Some 1,500 initial descriptions are mentioned (whereby numerous corrections had to be made in this respect). Such creative or innovative ideas have often led directly to significant progress or served as a new starting point for subsequent path-breaking developments. The notable achievements of earlier physicians or clinicians deserve great respect! Regrettably, such important scientists of the past tend to be forgotten in our fast-moving times. In this context, we would

do well to remember the 2,000-year-old tradition of hepatology.

For that reason, I took great care in revising the chapter on "History of Hepatology". With its 20 historical figures, which have never before been published together, this chapter represents a special feature for all interested readers.

The comprehensive selection of colour illustrations has been extended to 530, so that the textbook has become a real atlas of hepatology. The 320 tables have been designed in different shades and colours. All figures and tables have been integrated in the textflow, making this edition especially attractive. So the book itself is designed to lead from "seeing" to "understanding" and, ultimately, to diagnostic and therapeutic "doing".

I should like to express my special gratitude for all the friendly assistance and helpful advice to the pathologist Prof. Dr. H.P. Fischer (Bonn), the radiologist Prof. Dr. K. Rauber (Wetzlar) as well as the gastroenterologists Prof. Dr. R. Jakobs (Wetzlar) and Dr. G. Schmidt (Kreuztal). In addition, I wish to thank the numerous colleagues who offered their support in preparing the first and second editions and whose names appear in the respective prefaces (see pp X and XII). The abbreviations or symbols frequently used are listed in the preface to the first edition together with all other information regarding dictionary and technical terms.

All my personal thoughts and emotions, which are written down in the first and second edition, have constantly been with my beloved son Hans-Dieter. This comprehensive volume must be seen as our joint life's work.

My special thanks go to the company Pagina Media (Hemsbach) for their excellent setting of all three editions and for their most friendly collaboration over many years. Finally, I thank the employees at Springer Publishing House (Heidelberg) for completing this book, with special mention of Hinrich Küster, senior editor, and Meike Seeker, project manager, for their encouragement and kind support at all times.

Wetzlar, May 2008

Erwin Kuntz

#### Foreword to the third edition

"... because the liver is a source of many diseases, and is a noble organ that serves many organs, almost all of them: so it suffers, it is not a small suffering, but a great and manifold one" (Paracelsus, 1493–1541). • This quotation already appears as a motto for the German edition "Praktische Hepatologie" (1998) written by Erwin Kuntz and his deceased son Hans-Dieter (1997 †). Even with our present-day level of knowledge, it is not possible to give a better definition of the key role played by the liver and of the various clinical pictures involved, which require a holistic approach.

Despite the fact that "empirical liver research" can boast of a long and cult-related tradition dating back to Babylonian and ancient Egyptian times and although the liver and/or its components have always been an important subject of basic research, clinical hepatology is a relatively recent discipline. A large number of biochemical, cell-biological and metabolic respondent mechanisms were studied and developed in connection with the liver; however, it took time for the results to be applied to clinical practice. Clinical hepatology became more widespread mainly due to the social relevance of liver diseases, which resulted from the significance of the liver as the central metabolic organ and the fact that the liver is the principal target and modulator of environmental influences on the human organism (e.g. toxic substances, alcohol, infections, diet), including drug therapy. The need for experts in clinical hepatology has evolved due to recent developments, such as discovery and characterization of hepatitis viruses, more specific treatment of viral liver diseases, liver transplantation, adverse effects of obesity with associated nonalcoholic fatty liver disease and frequency of complications in chronic liver diseases rising with age of the affected patients. Drug-induced liver damage is the price for medical progress in today's world. In spite of modern concepts used in the design of medicines, the liver remains particularly sensitive to side effects due to its biotransformational function and the pharmacogenetic characteristics of each individual person.

In his foreword to the first English edition of "Hepatology. Principles and Practice", Charles S. Lieber praises it as an international landmark in the field of clinical hepatology. And rightly so! The concept was, and still is, innovative in many respects. This is confirmed by the worldwide success of the book and the fact that the first two editions were completely sold out. The third edition entitled "Hepatology. Textbook and Atlas" with its numerous figures and coloured tables is a further extension of the original concept. In order to understand liver diseases in more depth, it is essential to have a basic knowledge of morphology, pathology, physiology and molecular biology in a clinical context. This book does justice to present-day liver research (also known as "biomolecular hepatology") without losing sight of the patient as the main focus of all efforts.

The new edition comprises 40 chapters, each with its own detailed table of contents for easy reference. The individual chapters deal in a lucid manner with historical aspects, modern diagnostic methods (not forgetting the classical form of bedside examination: "One good feel of the liver is worth any two liver function tests" — F.M. Hanger jr.,

1971), symptomatology and general as well as specific effects of liver disease. The fluent and uniform style of presentation underlines the special value of a "one-author" book as opposed to "collective-author" books, which are more common today! Clearly structured information about aetiology, pathogenesis, clinical-pathological correlations, therapy and prognostic assessment helps the reader to gain a complete understanding of the material. A total of more than 500 figures turn the book into a true "atlas". All figures are excellently integrated into the textflow and literally illustrate the content. With the help of the high-quality laparoscopy- and histology-related figures, reading becomes a real pleasure, even for the pathologist. But it is not only the figures which give the book its "completeness". Another special feature are the historical aspects, which describe the development of hepatology up to the present day, and the general evolution of knowledge concerning the liver. This is achieved by stating the first-time authors of the respective clinical pictures, syndromes and advances in diagnostics, technology or therapy. The originators of relevant scientific theories are also mentioned.

The didactic approach which runs through the whole book is a clear indication of the author's immense practical experience in the field of hepatology as well as his understanding of the results of basic research, including the biological and pathological aspects which determine the given disease. Like Paracelsus, the author also looks beyond the liver in his deliberations. The reader also senses the long-term engagement of the author (and his son) in postgraduate education and the lessons learned from this. According to Papyrus Ebers (ca. 1550 BC), the liver is the "seat of emotions". And indeed, it is the emotions with which father and son began their undertaking that are clearly palpable and, at the same time, the key to success. It is only possible to impart knowledge and to convey enthusiasm if one has great personal involvement. This certainly applies to the authors, Erwin and Hans-Dieter Kuntz.

The current edition contains up-to-date information, but also stands for tradition and progress in hepatology. The reader is carefully introduced into the subject matter and learns to experience and understand everything to the full extent. Consequently, the book is not only a source of knowledge for the relatively small circle of hepatologists; due to the chosen form in which the material is presented, the book will surely arouse the interest of less specialized readers, including those involved in research. Thus this work serves as a starting point for new "liver enthusiasts". It is food for thought and a trigger for continued research. Our thirst for knowledge is unquenchable. This book lays out in an admirable fashion what is state of the art, but it makes no dogmatic statements. Therefore we have every reason to look forward to the next edition.

O. Univ. Prof. Dr. Helmut Denk, FRCPath Director of the Institute of Pathology University of Graz Auenbruggerplatz 25 A-8036 Graz (Austria)

#### Preface to the second edition

Originally, it was the intention of both my son and me that the German edition of "Praktische Hepatologie" should be followed by an English translation. After Hans-Dieter's premature death due to a serious illness, I made it my aim to complete an Englishlanguage version of the textbook by myself, knowing that this would have been his great wish. The memory of my dear son was an inspiration to me in my efforts at all times.

It was a great sense of achievement for both author and publisher that the first edition (2002) was sold out within such a short period and that a reprint was necessary. This fact, supported by the positive response shown directly by readers and reviewers, was the main motivation to prepare a second edition.

A decision was made to keep the well-established division of hepatology into six specialist areas; once again, forty chapters were used. Each chapter has been revised and updated with regard to content and language. At the beginning, there is a detailed table of contents and, at the end, a list of references. Like its predecessor, the second edition contains a visually comprehensive arrangement of the text into sections, incorporating various script sizes and types as well as 306 tables in half-tone colouring; significant conclusions are set in coloured boxes. A big, black dot is inserted whenever the following sentence represents a semantic leap from the preceding statement. (For further details regarding the structural concept of the chapters, see preface to 1st edition, page VII, paragraph 2.)

Altogether, about 7,000 references have been cited, of which some 1,500 have been replaced by more recent papers, including many from 2005. The Vancouverstyle layout has been used again, since it proved to be clear and easy to read. (For further details regarding the extensive bibliography, see preface to 1<sup>st</sup> edition, page VII, paragraph 3.)

Every effort has been made to maintain and improve the concept of citing, whenever possible, the first-time authors of syndromes, clinical entities, morphological or clinical findings, imaging or endoscopic techniques and conservative or surgical measures. (For further details, see preface to 1st edition, page VII, paragraph 4.)

The number of coloured figures has been increased by 97 to a total of 477; developments in printing

techniques make possible an even more colourful presentation with brilliant reproduction. All the figures are integrated in the text-flow. In this way, a hepatological atlas has been created, leading from "seeing" to "understanding", thereby facilitating diagnostic and therapeutic "acting".

My special thanks for their friendly assistance and helpful advice go to the pathologists Prof. Dr. H.-P. Fischer (Bonn) and Prof. Dr. G. Korb (Weiden), the radiologist Prof. Dr. K. Rauber (Wetzlar), the hepatologist Prof. Dr. J. Eisenburg (Munich), the virologist Prof. Dr. G. Berencsi (Budapest), the immunologist Prof. Dr. W. Storch (Weinheim) and the gastroenterologist Dr. G. Schmidt (Kreuztal). (In addition, numerous colleagues offered their support in preparing the first edition; they are named in the preface to 1st edition — see page VII, paragraphs 5 and 6.)

The abbreviations or symbols frequently used in the text are listed in the preface to the first edition (see page VIII).

All my personal thoughts and emotional feelings, which were written down in the first edition, are unchanged. This applies also to the two quotations from PARACELSUS at the beginning and end of the book. But, above all, how extremely happy and proud I would have been if my son Hans-Dieter could have joined me as co-author in achieving our common aim.

It is my sincere wish that this textbook will not only promote interest in the field of hepatology, but also deepen understanding of pathophysiological and morphological changes regarding liver as well as supporting successful application of the various diagnostic and therapeutic possibilities.

Finally, I should like to express my gratitude to the employees at Springer Publishing House (Heidelberg) for their professional help in completing this book, especially to Hinrich Küster, senior editor, and Meike Seeker, project manager, who gave their encouragement and kind support at all times.

Wetzlar, October 2005

Erwin Kuntz

#### Foreword to the second edition

The first edition of "Hepatology: Principles and Practice" by Erwin Kuntz, which appeared in 2002, was rapidly sold out. This was not astonishing since the textbook offered a comprehensive, lucid and scholarly presentation of liver disease. Informative figures and tables made reading a pleasure. The second edition has now been revised and updated to 2005 by Erwin Kuntz. Once again, the author, a distinguished hepatologist, has produced an encyclopedic masterpiece of hepatology. The book combines a complete scientific and historical discussion of the many aspects of hepatology together with the wise insight of a physician who has enormous practical experience in caring for patients with liver disease.

The second edition has been enlarged to more than 900 pages, a change necessitated by the enormous increase in our understanding of liver disease. The number of references that are cited now stands at 7,000; references are given in full and in alphabetical order, a feature that will prove most helpful to physicians engaged in teaching and research. The judicious use of color for figures and tables made the first edition extremely attractive to the reader. This practice is continued in the second edition which contains a further 97 figures and 30 tables, making a total of 477 figures and 306 tables. A special feature is the quality of the superb laparoscopic and histological pictures. Indeed, the colored figures are of such superior quality that they can be scanned directly for computer-based presentations. The histological illustrations are especially valuable as the number of autopsies and liver biopsies continues to decline worldwide. Moreover, these illustrations have been integrated perfectly into the text. The publishers, true to their long tradition, have done justice to the quality of this work in every way. The book is not only a true handbook of liver disease, but also a hepatological atlas.

Like its predecessor, the second edition also comprises 40 chapters. At the beginning of each chapter, there is a complete table of contents, which, together with the general index, makes it possible for the reader to find specific topics easily. The first chapter "History of Hepatology" is an indication of the depth and breadth of the knowledge which the author brings to the current edition. This chapter contains a richness of historical illustrations depicting

Ulrich F. Leuschner, M. D. Professor of Medicine, Johann Wolfgang Goethe University Frankfurt/M., Germany

the birth of knowledge of this multifaceted organ. The following chapters of the book show the profound knowledge and interest of Erwin Kuntz in the multiple spectra of hepatology. Each topic shows the evolution of our knowledge and acknowledges by name the individuals who contributed to our present knowledge. In this way, hepatology is not only discussed as a contemporary branch of internal medicine, but also related to the pioneering achievements of our ancestors, who deserve our full respect and recognition. The historical emphasis is global, rather than European. Throughout the book, detailed histological depictions of hepatic pathology have been fused with scientific aspects and clinical procedures. All forms of treatment have been updated, so that this work can be used as a manual of therapy which will be highly useful to both practitioners and teachers.

As Charles S. Lieber, New York, wrote three years ago in his foreword to the first edition, such a text-book could not have appeared at a better time. This statement applies to the second edition in the year 2005. Great progress has been made in hepatology with regard to diagnostics and therapy, and consequently, the number of publications dealing with, for example, the treatment of viral hepatitis has grown immensely. Likewise, there is much new information on the pathogenesis of autoimmune liver diseases and so-called overlap syndromes. Thus it is essential that the current body of knowledge is presented in an intensive and accurate form.

It is a pleasure to know Prof. Dr. Erwin Kuntz personally. His enthusiasm for hepatology is contagious and can be sensed in every chapter. To be shown his enormous private library and pictorial archive is a moving experience. This impressive collection contains important papers and original monographs of authors from past and present and provides the data base for this fascinating textbook.

We would like to wish this new edition from Erwin Kuntz the same resounding success which was enjoyed by the first edition. We are convinced that the book will not only find its place in every medical library, but also be consulted repeatedly by scientists and physicians who seek to understand how we can use its contents to improve the care of our patients with liver disease.

Alan F. Hofmann, M. D. Professor Emeritus of Medicine University of California, San Diego La Jolla, USA

### Preface to the first edition

It is a wonderful experience for a father to work with his son on an enormous number of lectures, seminars, courses, congresses and publications over a period of many years. For a total of 35 (overlapping) years we were both active as clinicians in the field of hepatology. From this experience arose our wish to co-author a book on this fascinating subject. We were greatly encouraged in this project by friends and colleagues. • The joint work, supported by an extensive personal archive, a large number of clinical, endoscopic and morphological illustrations, and documentation of imaging technique findings, is intended to serve as a teaching manual, a textbook, and a reference book – for use in the doctor's surgery, in daily clinical practice, and in the specialist fields associated with hepatology.

After weighing up the various approaches and objectives of the book, the *concept* of subdividing the subject matter into 40 self-contained chapters presented itself. We set value on: - a systematic structure of the chapters, - a coherent presentation of facts and evidence, – a visually comprehensible arrangement of the text into sections, incorporating various script sizes and types, – half-tone colouring of tables and conclusions considered to be of exceptional importance, – consistent cross-referencing of figures, tables and text between different chapters, and the incorporation within the text of 276 tables, 380 figures, and numerous boxed texts (all in colour). • A big, black dot is inserted whenever the following sentence represents a mental leap from the preceding statement, which enables a more structured approach. • Our constant aim was to improve the readability and clarity of the book.

Each chapter has an extensive bibliography. We used a modified Vancouver-style layout, which we consider clear and easy to read. Authors' names (all authors are listed in full in the chapter bibliography) appear in semi-bold type and are ordered alphabetically for easy reference. As far as possible, we subdivided more extensive chapter bibliographies thematically. A total of 7,300 publications up to 2001 are cited. This detailed bibliography is intended to assist the interested reader in exploring specific areas in more depth. • We have therefore included both historical references and those older publications which we consider of particular significance or interest – there is always the danger, in hepatology as well as in other fields, that such works might regrettably become victims of our fast-moving times. There is certainly a subjective influence in this selection, and in this context any additions or corrections to the bibliography will be gratefully received.

A further conceptual concern was to cite, whenever possible, the first authors of publications on syndromes, clinical research, laboratory parameters, imaging or endoscopic techniques, morphological findings of special interest, and conservative, invasive and surgical procedures (and to correct previous information given in the literature). In the past, the creative or innovative ideas of these inaugurators have often led directly to significant progress or have served as a new starting point for subsequent, ground-breaking developments. Despite arduous research, it has not always been possible to attribute work correctly to the first author(s). Yet, the notable achievements of earlier physicians, clinicians and scientists deserve to be remembered with respect! In this connection, further information or corrections will be welcomed.

The extensive selection of *colour illustrations* incorporated into the text covers a wide range of clinical and morphological findings in hepatology: it is designed to lead from "seeing" to "understanding", thereby facilitating diagnostic and therapeutic "acting". Although we had collected an extensive picture archive of our own over a period of more than 30 years of clinical practice, we were nevertheless able to complement this and close any gaps thanks to numerous illustrations and impressive findings generously made available to us by colleagues. My special thanks for their friendly assistance go to the pathologists Prof. Dr. H.-P. Fischer (Bonn) and Prof. Dr. O. Klinge (Kassel), and to the radiologists Prof. Dr. K. Rauber (Wetzlar) and Prof. Dr. R. Heckemann (Bochum). Some very valuable documentations of findings could be used by courtesy of Prof. Dr. J. Eisenburg (Munich), Prof. Dr. K.-M. Müller (Bochum), Prof. Dr. G. Piekarski (Bonn), Prof. Dr. H. Thaler (Vienna), Prof. Dr. G. Volkheimer (Berlin), Prof. Dr. O. Vorländer (Berlin), and Prof. Dr. W. Wermke (Berlin).

We repeatedly enlisted the *helpful advice* of friends and colleagues to supplement or confirm our own interpretations. Our opinions not infrequently diverged (and in the field of hepatology, this can only be an advantage) and personal opinions were modified or confirmed. The contacts arising from these discussions have been immensely rewarding to me. Here I should like to express my special thanks to: Prof. Dr. G. Berencsi (Budapest), Prof. Dr. R. Klein (Tuebingen), Prof. Dr. H. K. Seitz (Heidelberg) and Prof. Dr. W. Storch (Weinheim). • Very many thanks for advisory support also go to: Prof. Dr. H.-R. Duncker (Institute of Anatomy, Univ. of Giessen), Priv. Doz. Dr. Marietta Horster (Institute of Classics and Ancient History, Univ. of Cologne) and Prof. Dr.

N. Katz (Institute of Biochemistry, Univ. of Giessen).

• Receiving such varied and kind assistance and advice has filled me with gratitude and encouragement during the years spent compiling this book.

In preparing the book my thoughts and my loving gratitude have constantly been with *my son*, *Hans-Dieter*, whose death was so sudden and incomprehensible to us all. I have tried to represent his inspirations and detailed ideas as well as incorporating his particular clinical insights. This volume is thus our joint life's work. He will always be remembered as an example to us all.

At the beginning and end of the book I have purposely cited two quotations from PARACELSUS which have always made a deep impression on me. • In the course of such intensive engagement with the history of hepatology, one is repeatedly filled with respect and admiration for how our forebears, solely through sight, hearing and touch, and an ingenuity of methods — and through logical deduction — drew medical conclusions, recognized correlations and established

an astounding body of theoretical and practical knowledge. Many of these empirical findings were subsequently confirmed – some (still) remain "empirical", without, however, having been disproved. "Empiricism, Intuition and Logic" (R. Gross, Cologne, 1988) will always be the leitmotif of the physician! • The considerable and fascinating developments in hepatology, especially those of the last ten years, remain a central theme. • The current stage of this development may well become known as the 4<sup>th</sup> (biomolecular) epoch of hepatology, as I have proposed in the first chapter of our book.

Finally, my thanks to the employees at *Springer* for the speedy completion of this book and especially to Jörg Engelbrecht and Dr. Dorothee Guth for their encouragement and kind support at all times.

Wetzlar, July 2001

Erwin Kuntz

Frequently used *abbreviations* and *symbols* in the textbook are listed in alphabetical order below:

s. fig. s. figs. s. p.	see figure see figures see page	ca. e. g. etc.	circa exempli gratia, for example et cetera, and so on	av. N.B. i. m.	arterio-venous nota bene, important intramuscular
s. 11gs. s. p. s. pp s. tab.	see figures see page see pages see table	e.g. etc. i.e. quot.	exempli gratia, for example et cetera, and so on id est, that is quoted, quotation	N.B. i. m. i. v. s. c.	intramuscular intravenous subcutaneous
s. tabs.	see tables	VS	versus	V. V.	vice versa, conversely

As regards the *half-tone colouring* and colour intensity, blue is used — as far as possible — for normal findings, classification, causes, indications, therapy regimen, etc., red applies to pathological findings, contraindications, complications, side effects, etc., yellow to methods, test procedures, etc., and grey to historical details.

Medical and technical terms, orthography and hyphenation in this textbook are based on: (1.) P. Procter (editor): Cambridge International Dictionary of English (Cambridge Univ. Press) 1999, 3<sup>rd</sup> edition; (2.) J. Crowther (editor): Oxford Advanced Learner's Dictionary (Oxford Univ. Press), 1999, 5<sup>th</sup> edition; (3.) J. Dorland, W.A. Newman (editors): Illustrated Medical Dictionary (W.B. Saunders, Philadelphia, et al.), 2000, 29<sup>th</sup> edition; (4.) F.J. Nöhring (editor): Langenscheidt's Fachwörterbuch Medizin (Langenscheidt, Berlin, et al.), 1996, 3<sup>rd</sup> edition; (5.) W.E. Bunjes (editor): Medical and Pharmaceutical Dictionary (Thieme, Stuttgart, et al.), 1985, 4<sup>th</sup> edition; (6.) S. Dressler (editor): Dictionary of Clinical Medicine (Chapman & Hall, London, et al.), 1996.

#### Foreword to the first edition

The textbook "Hepatology. Principles and Practice" by Erwin Kuntz and Hans-Dieter Kuntz will undoubtedly become an international landmark. It reflects the scholarship, encyclopedic knowledge of the authors and the outstanding craftsmanship of the publishers. Professor Erwin Kuntz's stature was not only well established in Germany and the rest of Europe but his fame had crossed the Atlantic and I have known of him for many years. I also had the privilege of getting acquainted with him personally at an international meeting on phospholipids in Cologne in 1989 where I had the pleasure of enjoying both his intellectual and his broad humanistic qualities.

The book is not only an unusual combination of an extremely thorough textbook of all aspects of hepatology, including important pathogenic mechanisms and their clinical application, but it also has a very didactic approach which effectively highlights most points while not neglecting those details the academician or practitioner may want to find for needed clarification. It synthesizes more than 30 years of practical experience in clinical hepatology. Accordingly, it can be used as a teaching manual for students, postgraduate clinicians and practitioners, as a textbook for internists, gastroenterologists and hepatologists, as well as a reference book for teachers, scientists and authors. The original text has been revised and updated to 2000/2001. The bibliography now consists of about 7,300 papers and the number of colored figures has been increased to 380. It is a distillate of hundreds of personal publications and presentations and thousands of literature references of classic and contemporary scholars. The information is presented

in such a way that it makes the facts very accessible and the chore of retrieval becomes a pleasure. The very vivid display of information gives unique insights providing a very rational approach to the practice of hepatology. This volume brilliantly achieves the basic aim of its authors, which is to guide the user from "seeing" to "understanding" and finally to "acting".

The book could have come at no better time. There is real blossoming of hepatology worldwide and its importance has increased logarithmically with the availability of transplantation and the pandemic of hepatitis C, with effective treatments finally evolving. Diagnostic procedures have also gained much greater sophistication and "interventional" hepatology is now finally on the rise. Being familiar with German, I had the pleasure of enjoying the original textbook but felt envious that this opus was limited to those fluent in that language. I am delighted to see that this work will now be shared worldwide in an English edition which has been thoroughly updated, with the most recent concepts and therapies reported and carefully assessed. Its comprehensive yet crisp and clear presentation will open the gates of hepatology to all health professionals. Last but not least, this work represents the highly humanistic qualities of its authors and is obviously an act of life time love, with abundant citations not only to our modern masters, but also giving proper credit to those who preceded them. Hippocrates already stated that the liver was the site of the soul; it is obvious that both Erwin Kuntz and his son, Hans-Dieter, have put their souls in this opus.

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# Abbreviations -

Abbreviation:	Meaning:	Abbreviation:	Meaning:
A		BLSS	Bioartificial liver support system
2 %		BMI	Body mass index
AA	Amino acid	BMP	Bone morphogenetiv factor
AAA	Acitiactin antibody	BRIC	Benign recurrent intrahepatic cholestasis
AAA	Aromatic amino acid	BSEP	Bile salt export pump
AAT	$\alpha_1$ -antitrypsin	BSR	Blood sedimentation rate (= ESR)
ABT	Aminopyrine breath test	BUN	Blood urea nitrogen
AcCoA	Acetyl coenzyme A	BW	Body weight
ACE	Angiotensin-converting enzyme		
ACTH	Adrenocorticotropic hormone	C	
ADI	Adenofir Antidiuretic hormone	C	
ADH ADH	Alcohol dehydrogenase	CAGE	Alcoholism test
ADP	Adenosine diphosphate	CAH	Chronic active hepatitis
ADR	Adverse drug reaction	CAM	Cell adhesion molecule
ADT	Placebo (any – what you desire – thing)	cAMP	Cyclic adenosine monophosphate
AE	Anion exchanger	CBAT	Canalicular bile acid transporter
AFP	$\alpha_1$ -foetoprotein	CBG	Corticosteroid-binding globulin
Ag	Antigen	CC	Cystadenocarcinoma
AHA	Antibody histone (2B)-A	CCC	Cholangiocellular carcinoma
AIC	Autoimmune cholangitis	CDCA	Chenodeoxycholic acid
AIH	Autoimmune hepatitis	CDK CDT	Cyclin-dependent kinase Carbohydrate-deficient transferrin
AIP	Acute intermittent porphyria	CEA	Carcinoembryonic antigen
ALA	δ-aminolaevulinic acid	CEDS	Colour-encoded Doppler sonography
ALAD	δ-aminolaevulinic acid-dehydratase	CEP	Congenital erythropoietic porphyria
ALD	Aldolase	CESD	Cholesterolester storage disease
ALD	Alcohol liver disease	CET	Caffeine elimination test
ALDH	Aldehyde dehydrogenase	CETP	Cholesterolester transfer protein
ALF	Acute liver failure	CEUS	Contrast-enhanced ultrasonography
ALG	Antilymphocytic globulin	CF	Cystic fibrosis
ALL	Acute lymphatic leukaemia	CFR	Complement fixation reaction
ALT AMA	Alanine aminotransferase (= GPT) Antimitochondrial antibody	CFT	Complement fixation test
AML	Acute myelogenous leukaemia	CFTR	Cystic fibrosis transmembrane regulator
AMP	Adenosine monophosphate	cGMP	Cyclic guanosine-3', 5'-monophosphate
ANA	Antinuclear antibody	CH	Cavernous haemangioma
ANCA	Antineutrophil cytoplasmic antibody	ChE	Cholinesterase
ANF	Atrial natiuretic factor	CHBV	Crane hepatitis B virus
AP	Alkaline phosphatase	CHP	Chronic hepatic porphyria
APOLT	Auxiliary partial orthotopic liver transplantation	CIBD CLH	Chronic inflammatory bowel disease Chronic lobular hepatitis
APTT	Activated partial thromboplastin time	CLL	Chronic lymphatic leukaemia
APUD	Amine precursor uptake and decarboxylation	CM	Contrast medium
ARA-AMP	Adenine arabinoside monophosphate	CML	Chronic myeloid leukaemia
ARP	Anti-ribosomal P antibody	CMV	Cytomegalovirus
ASA	Acetylsalicylic acid	CNDC	Chronic non-suppurative destructive cholangitis
ASGPR	Asialoglycoprotein receptor	CNS	Central nervous system
ASH	Alcoholic steatohepatitis	CO	Cardiac output (vol./min)
AST AT III	Aspartate aminotransferase (= GOT) Antithrombin III	CPH	Chronic persistent hepatitis
ATP	Adenosine triphosphate	CREST	Calcinosis-Raynaud-esophagus-sclerodactyly-
ATPase	Adenosine triphosphatase		telangiectasia syndrome
AVP	Arteriovenous pressure	CRP	C-reactive protein
AWS	Alcohol withdrawal syndrome	CSF	Cerebrospinal fluid
11115	Theoret Witherawar Syndrome	CSH	Chronic septal hepatitis
		CSI	Cholesterol saturation index
В		CT CTAP	Computer tomography
DAC	Pland alashal apparation		CT arterioportography
BAC	Blood alcohol concentration Bioartificial liver device	CTL CVP	Cytotoxic T lymphocyte Central venous pressure
BAL BBB	Blood-brain barrier	CYP	Cytochrome P-450
BCAA	Branched-chain amino acid	C11	Cytoemonic 1 130
BCS	Budd-Chiari syndrome		
BELS	Berlin extracorporeal liver support	D	
BICAP	Bipolar circumactive probe	DBP	Vitamin D-binding protein
2.0	r		

		TT	
DCP	Des-gamma-carboxy prothrombin	H	
DCP DDT	Divalent cation transporter Dichlorodiphenyltrichloroethane	HAI	Hepatitis activity index
DHBV	Duck hepatitis virus	HAV	Hepatitis-A virus
DIC	Disseminated intravascular coagulation	HBDH	α-Hydroxybutyrate dehydrogenase
DLPC	Dilinoleoylphosphadidylcholine	HBIG	Hepatitis-B immunoglobulin
DNA	Deoxyribonucleic acid	HBP	Hepatic binding protein
DOD	Degree of disability	HBSS HBV	Hepatobiliary sequence scintigraphy Hepatitis-B virus
DRQ	DeRitis quotient	HCC	Hepatocellular carcinoma
DSA	Digital subtraction angiography	HCP	Hereditary coproporphyria
		HCV	Hepatitis-C virus
E		HDL	High-density lipoprotein
EBV	Epstein-Barr virus	HDV	Hepatitis-D virus
EC	Elimination capacity	HE	Haemotoxylin eosin
ECLP	Extracorporeal liver perfusion	HE	Hepatic encephalopathy
ECM	Extracellular matrix	HEP HES	Hepatoerythropoietic porphyria Hydroethyl starch
ECP	Erythropoietic coproporphyria	HEV	Hepatitis-E virus
ECS EDRF	Extracellular space Endothelium-derived relaxing factor	hFABP	Hepatic fatty acid-binding protein
EDTA	Ethylenediaminetetraacetic acid	HGBV	Hepatitis-GB virus
EEG	Electroencephalography	HGF	Hepatocyte growth factor
EEP	Endogenous evoked potentials	HGV	Hepatitis-G virus
EGF	Epidermal growth factor	HHBV	Heron hepatitis B virus
EHP	Erythrohepatic porphyria	HHC	Hereditary haemochromatosis
EHT	Electrohydrothermic probe	HHT HHV	Hereditary hepatic telangiectasia Human herpes virus
ELAD	Enzyme immunoassay	HIDA	Hepatic iminodiacetic acid
ELAD ELISA	Extracorporeal liver assist device Enzyme-linked immunosorbent assay	HIV	Human immunodeficiency virus
EPL	Essential phospholipids	HL	Half-life
EPP	Erythropoietic protoporphyria	HLA	Human leucocyte antigen
ER	Endoplasmic reticulum	HLT	Heterotopic liver transplantation
ERC	Endoscopic retrograde cholangiography	HMG-CoA	Hydroxymethylglutaryl-CoA
ET	Endothelin	HMV	Heart minute volume
EUS	Endoscopic ultrasound	HNF	Hepatocyte nuclear factor
EvG EVR	Elastica van Gieson	HPI HPLC	Hepatic proliferation inhibitor High-pressure liquid chromatography
EVK	Early viral response	HPS	Hepatopulmonary syndrome
		HRGP	Histidine-rich glycoprotein
F		HRQL	Health-related quality of live
FA	Fatty acid	HRS	Hepatorenal syndrome
FBP	Folate-binding protein	HSS	Hepatic stimulatory substance
FENa	Fractional sodium excretion	HSV	Herpes simplex virus
FFA	Free fatty acid	HTL	Hepatic triglyceride lipase
FFP FGF	Fresh frozen plasma Fibroblast growth factor	HVF HVPG	Hepatocyte volume fraction Hepatic vein pressure gradient
FHCC	Fibrolamellar hepatocellular carcinoma	11110	Trepatie vein pressure gradient
FHF	Fulminant hepatic failure (= ALF)		
FHVP	Free hepatic venous pressure	I	
FIA	Fluorescence immunoassay	IBC	Iron-binding capacity
FM	Fibrin monomer	IBP	Iron-binding protein
FNB FNH	Fine needle biopsy Focal nodular hyperplasia	ICAM	Intercellular adhesion molecule
1.1111	rocai nodulai nyperpiasia	ICDH	Isocitrate dehydrogenase
		ICG	Indocyanine green
$\mathbf{G}$		ICP	Intracranial pressure
GABA	Gamma-aminobutyric acid	ICS	Intracellular space
GBV	GB-Virus	ICU	Intensive care unit
GDH	Glutamate dehydrogenase	IDL IDUS	Intermediate density lipoprotein Intraductal ultrasound
GEC GFR	Galactose elimination capacity Glomerular filtration rate	IFN	Interferon
GGT	Gamma-glutamyl transpeptitase	IFT	Immunofluorescence test
GHRF	Growth hormone-releasing factor	IGF	Insulin-like growth factor
GMCSF	Granulocyte macrophage colonic stimul. factor	IHAT	Indirect haemagglutination test
GOT	Glutamic oxaloacetic transaminase (= AST)	IL	Interleukin
GPT	Glutamic pyruvic transaminase (= ALT)	INR	International normalization ratio
GSH	Reduced glutathione	IOUS IRF	Intraoperative ultrasound
GSHV GSSG	Ground squirrel hepatitis virus Oxidized glutathione	ISAGA	Iron regulation factor Immunosorbent agglutination assay
GST	Glutathione-S-transferase	ISC	Iron saturation capacity
GVHD	Graft-versus-host disease	IU	International unit

K		N	
KB	Ketone bodies	NAD	Nicotinamide adenine dinucleotide
kDa	Kilo-Dalton	NADP	Nicotinamide adenine dinucleotide phosphate
KKS	Kallikrein-kinin system	NAFLD	Non-alcoholic fatty liver disease
		NALD	Non-alcoholic liver disease
$\mathbf{L}$		NASH	Non-alcoholic steatohepatitis
L		NCT	Number-connection test
LAM	Lamivudine	nDNA NHL	Nuclear DNA
LAP	Laparoscopy	NHL NLCT	Non-Hodgkin lymphoma Number-letter combination test
LAP	Liver active protein	NO	Nitrous oxide
LAP	Leucine aminopeptidase	NRH	Nodular regenerative hyperplasia
LASER	Light amplification by stimulated emission of radiation	NSAR	Non-steroidal antirheumatics
LB	Liver biopsy	NU	5'-Nucleotidase
LC1	Liver cytosol typ 1 antibody		
LCAT	Lecithin-cholesterol acyl transferase	O	
LCT	Lipiodol-computer tomography	O	
LD	Lethal dose	OA	Ornithine aspartate
LDH	Lactate dehydrogenase	OATP	Natrium-independent transport system for
LDL	Low-density lipoprotein		organic anions
LDLT	Living donor liver transplantation	OCT	Ornithine carbamoyltransferase
LE	Lupus erythematosus	OGTT	Oral glucose tolerance test Overlap syndrome
LFA LFT	Lymphocyte function antigen Liver function test	OLS OLT	Orthotopic liver transplantation
LIP	Liver inhibitor protein	ORF	Open reading frame
LITT	Laser-induced thermotherapy	ORI	open reading frame
LKM	Liver-kidney microsomal antigen		
LMA	Liver membrane autoantibody	P	
LPA	Liver-pancreas antibody	PAF	Platelet-activating factor
LPL	Lipoprotein lipase	PAH	Para-aminohippuric acid
LP X	Lipoprotein-X	PAI	Percutaneous acetic acid injection
LR	Liver resection	PAI	Plasminogen activator inhibitor
LSP	Liver-specific protein	PAIR	Punction/Aspiration/Injection/Re-Aspiration
LT LTC	Liver transplantation  Laparoscopic transhepatic cholangiography	pANCA	Perinuclear antineutrophilic cytoplasmic antibody
LTT	Line-tracing test	PAP	Pulmonary artery pressure
LTT	Lymphocyte transformation test	PAS	Para-aminosalicylic acid
LWW	Liver wet weight	PAS	Periodic acid-Schiff reaction
	3	PBC PBG	Primary biliary cholangitis/cirrhosis
3.4		PCB	Porphobilinogen Polychlorinated biphenyl
M		PCNA	Proliferating cell nuclear antigen
MALT	Munich alcoholism test	PCO <sub>2</sub>	Partial pressure carbon dioxide
MALT	Mucous membrane associated lymphoid tissue	PCP	Pentachlorophenol
MAO	Monoamine oxidase	PCR	Polymerase chain reaction
MARS	Molecular adsorbend recirculatory system	PCT	Porphyria cutanea tarda
MAST	Michigan alcoholism screening test	PCWP	Pulmonary capillary wedge pressure
mAST	Mitochondrial aspartate aminotransferase	PDGF	Platelet-derived growth factor
MBq	Megabecquerel Midclavicular line	PDR	Plasma disappearance rate
MCL MCT	Medium-chain triglyceride	PEEP PELAM	Positive end-expiratory pressure Platelet endothelial cell adhesion molecule
MCV	Mean corpuscular volume	PEI	Percutaneous ethanol injection
MEGX	Monoethylglycinexylidide test	PEM	Protein-energy malnutrition
MELD	Model for endstage liver disease	PET	Positron emission tomography
MELS	Modular extracorporeal liver support	PG	Prostaglandin
MEOS	Microsomal ethanol-oxidizing system	PHI	Phosphohexose isomerase
MFH	Malignant fibrous histiocytoma	Pi	Protease inhibitor
mGOT	Mitochondrial glutamic-oxalacetic transaminase	P III-P	Procollagen-III-peptide
MHC	Major histocompatibility complex	PMN	Polymorphonuclear neutrophilic leucocytes
MIGET	Multiple inert gas elimination technique	PPC	Polyenylphosphatidylcholine
MMF MMP	Mycophenolate mofetil Matrix metalloproteinase	PPH PPSB	Primary pulmonary hypertension Prothrombin complex (prothrombin, procon-
MOAT	Multi-organic anion transporter	1130	vertin, Stuart factor, antihaemophilic factor B)
MPS	Mononuclear phagocyte system	PSC	Primary sclerosing cholangitis
MRC	Magnetic resonance cholangiography	PSE	Portosystemic encephalopathy
MRI	Magnetic resonance imaging (= MRT)	PT	Prothrombin time (= Quick)
mRNA	Messenger RNA	PTC	Percutaneous transhepatic cholangiography
MRP	Multi-drug resistance protein	PTH	Parathormone
MT	Metallothionein	PTP	Percutaneous transhepatic portography
MTP	Microsomal triglyceride transfer protein	PTT	Partial thromboplastin time

PVC PVS	Polyvinyl chloride Peritoneovenous shunt	TACE TAE TBG	Transarterial chemoembolization Transarterial embolization Thyroxine-binding globulin
Q QOL	Quality of life	TCDD TGF TIBC TIMP TIPS TNF	Dioxin Transforming growth factor Total iron-binding capacity Tissue inhibitor metalloproteinase Transjugular intrahepatic portosystemic shunt Tumour necrosis factor
RAAS RAST RBP RCE REE RER RES RFA RFTA RHS	Renin-angiotensin-aldosterone system Radio-allergo-sorbent test Retinol-binding protein Reduction in earning capacity Resting energy expenditure Rough endoplasmic reticulum Reticuloendothelial system Radio frequency ablation Radiofrequency thermal ablation Reticulohistiocytic system Radioimmunoassay	TNM  tPA TPT TRH tRNA TSH TT TTR TUDCA TVC	Malignant tumour classification system (tumour, node, metastasis) Tissue plasminogen activator Thromboplastin time Thyreotropin-releasing hormone Transfer RNA Thyroid-stimulating hormone Thrombin time Transthyretin Tauro-ursodeoxycholic acid Transvenous cholangiography
RIBA RNA RNF ROI rRNA RT-PCR	Recombinant immunoblot assay Ribonucleic acid Renal natriuretic factor Reactive oxygen intermediates Ribosomal RNA Reverse transcription-polymerase chain reaction  S-adenosylmethionine	UUDCA UDP UES uPA US UTP UV UW	Ursodeoxycholic acid Uridine diphosphate Undifferentiated embryonal sarcoma Urokinase plasminogen activator Ultrasound Uridine triphosphate Ultraviolet University of Wisconsin solution
SBP SDH SeHCAT SEP SER SLA SLT SMA SOD SOL SPECT SPIO SQUID SSC	Spontaneous bacterial peritonitis Sorbitol dehydrogenase Selenohomotaurocholic acid test Somatosensory evoked potentials Smooth endoplasmic reticulum Soluble liver antigen Split liver transplantation Smooth muscle antibody Superoxide dismutase Space-occupying lesion Single-photon emission computer tomography Superparamagnetic particles of iron oxide Superconducting quantum-interference device Secondary sclerosing cholangitis	V VBDS VC VCAM VEGF VEP VIP VLDL VOD VZV	Vanishing bile duct syndrome Vinyl chloride Vascular cell adhesion molecule Vascular endothelial growth factor Visually evoked potentials Vasoactive intestinal polypeptide Very low-density lipoprotein Veno-occlusive disease Varicella-zoster virus
STD STH STP SVR	Sexually transmitted disease Somatotropic hormone Standard temperature (0 °C) and pressure (760 mg Hg) Sustained viral response	WAIS WHV WHVP WNV	Wechsler adult intelligence scale Woodchuck hepatitis virus Wedged hepatic venous pressure West Nile virus
TAC	Transarterial chemotherapy	Y YF	Yellow fever

"... because the liver is a source of many diseases, and is a noble organ that serves many organs, almost all of them: so it suffers, it is not a small suffering, but a great and manifold one"

Theophrastus Bombastus von Hohenheim, known as Paracelsus (1493–1541)

(Liber tertius paramiri, de morbis ex Tartaro. St. Gallen, 1531)

The first and the last page of this book on hepatology (1st German edition 1998; 1st, 2nd and 3rd English edition 2002, 2004, 2008) are devoted to *Theophrastus Bombastus von Hohenheim*, called **Paracelsus**. The life and work of this great man have fascinated me since my youth.

Therefore, it was an indescribable feeling for me when, in 2006, I was awarded the **Paracelsus Medal** as the greatest distinction of the German Medical Profession It bears the inscription (see last page in all editions!) "the highest ground is love", which is part of a well-known quotation of Paracelsus himself concerning the benefit of remedies.

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