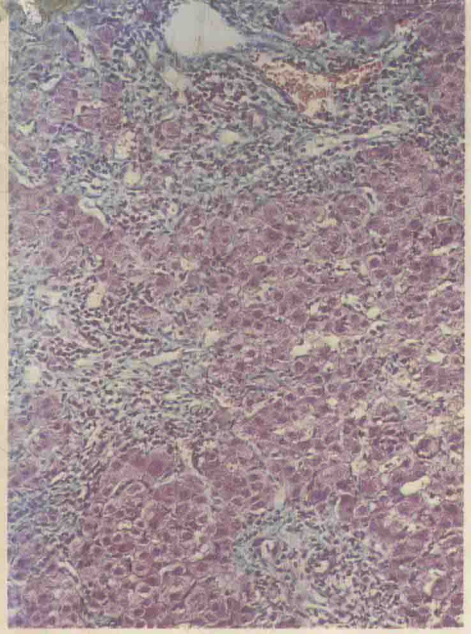

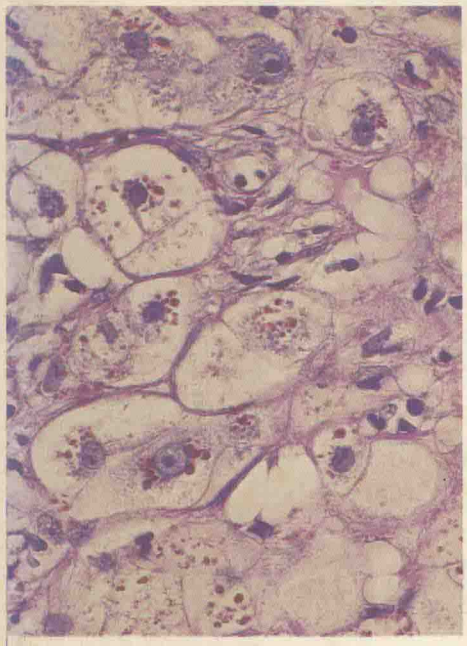

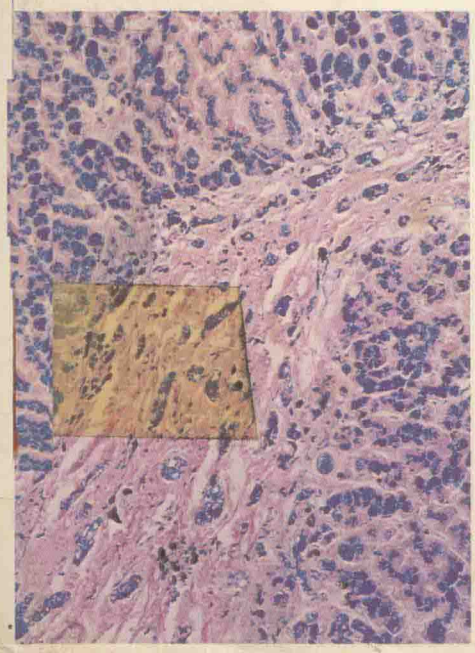

Color Atlas of Liver Biopsy: A Clinical Pathological Guide

Pedro J. Grases and Simón Beker G.

Alan R. Liss, Inc., New York

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Alan R. Liss, Inc., New York

Address all Inquiries to the Publisher
Alan R. Liss, Inc., 150 Fifth Avenue, New York, NY 10011

Printed in the United States of America.

Library of Congress Cataloging in Publication Data

Grases, Pedro J
Color atlas of liver biopsy.

Rev. translation of the authors' Guía práctica de biopsia hepática en el adulto.
Includes bibliographical references and index.
1. Liver – Biopsy – Atlases. 2. Histology, Pathological – Atlases. I. Beker G., Simón, joint author. II. Title. [DNLM: 1. Biopsy. 2. Liver diseases – Diagnosis. 3. Liver – Pathology. WI 700 G767g]
RC847.G6713 616.3'620758'0222 80-28801
ISBN 0-8451-0209-5

Color Atlas of Liver Biopsy: A Clinical Pathological Guide

Dedicated to the closest members of our families.

FOREWORD TO THE FIRST EDITION

The earliest classifications and clinicopathological correlations in liver disease were founded on the gross appearance of the liver at autopsy. When histological examination of the liver was introduced in the nineteenth century, classifications and correlations had their modern beginnings, and probably the greatest advances were made in our understanding of diseases of the liver. Soon physiological studies surpassed morphological ones in contributing to our knowledge of liver function in health and disease, particularly since such studies could be performed in the living patient, and the role of morphology was eclipsed. However, physiological investigation often failed to distinguish the many etiologies of hepatic dysfunction and, furthermore, results often failed to correlate well with either the clinical status of the patient or the prognosis. They also proved to be inadequate guides for therapy.

The invention of needle biopsy of the liver at the beginning of World War II produced a renaissance of morphology in the evaluation of liver disease. Clinicopathological correlations and classifications of diseases, as well as delineation of stages in individual diseases, could now be precisely made. More recently the extension of morphology to ultrastructure by application of electron microscopic, histochemical, and immunocytochemical techniques has greatly refined our understanding of physiological and pathological processes, and in some cases, the application of these techniques is even providing information about etiology. Much is expected from the general application of these new tools, as well as from biochemical examination of biopsy tissue.

A serious shortcoming exists, however, which must be overcome before the benefits of progress can be enjoyed by all the patients afflicted with diseases of the liver and by the physicians who care for these patients. The simplification of the biopsy procedure by the introduction of the thin-walled needle by Menghini has made liver biopsy a universally applied form of examination. Many pathologists, some schooled in the prebiopsy era, and some with little experience or training in interpreting the tiny slivers of tissue obtained with the needle, have great difficulty in providing the clinician with the information he seeks – information that is indeed usually in the specimen, needing only the trained eye to ferret it out. Patients are placed at risk with little likelihood of obtaining reliable data. Too many biopsies are now being performed to make a central registry feasible or even desirable. Therefore, an alternative pathway is suggested by providing "on-the-job" training of pathologists. Such training can be provided to the pathologists by having them use well-illustrated atlases as guides to help them in biopsy interpretation, and to suggest the clinical and functional correlations they should expect.

This present Practical Guide to Liver Biopsies in Adults, by Pedro Grases and Simón Beker, is an attempt to provide such a tool for pathologists in Spanish-speaking countries. Similar volumes are available in English, German, French, Russian and probably several other languages. The need is worldwide and great. The present guide also follows the current widely accepted nomenclature, so that problems in communication will be minimized. This is not the first such guide to be published in Caracas. In 1960 Valencia-Parparcen prepared one that first appeared in GEN and later was published as a separate booklet. The present volume, therefore, is a second-generation effort.

New books of any type must have something special to make them attractive to their users. In the case of this guide, the Spanish language and the excellent format would probably be sufficient reason for many to use it. It has, however, a remarkable additional virtue that will greatly widen the readership of the book, and one that should serve as a model for other authors. This virtue is the beauty of the color plates. These plates represent color photomicrography at its acme.

The guide will serve as a fine visual supplement to the new treatise of nomenclature of disease of the liver being prepared for the World Health Organization by the John E. Fogarty, International Center for Advanced Study in Health Sciences of the United States, National Institutes of Health, under the leadership of Drs. Carroll M. Leevy, Sheila Sherlock, and Hans Popper.

This foreword must have a personal note. The authors and their many colleagues of the Central University of Caracas are old friends

of mine. I feel that this volume represents their firm commitment to remain in the forefront of Latin American, and even in world, hepatology. Venezuelan hepatology owes much of its origin and present standing to Joel Valencia-Parparcen. Those who began as his students have now risen to positions of leadership, a natural step in growth and development. In appreciation of their efforts in this process of evolution, Pedro Grases and Simón Beker deserve commendation for a difficult task superbly done.

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July, 1974

ACKNOWLEDGMENTS

We should like to express our gratitude to Mr. Jesús E. Maldonado, from the Audiovisual Department of our School of Medicine (U.C.V.), for the photographic work, and to Miss Irma Petit, assistant technician of our institute, for her competence in preparing the histological sections. Our thanks are also extended to Mrs. Carol Lopez for revising the manuscript and to Mrs. Miriam G. de Sánchez for her secretarial support.

We could not fail to mention our appreciation for the kindness of the following colleagues who made available some of the illustrations: Isaac Almosny, MD, Hospital Vargas – Caracas (Fig. 45); Alberto Angulo O., MD, Instituto Nacional de Tuberculosis – Caracas (Fig. 84); Néstor Arreaza Colizza, MD, Hospital Privado "Centro Médico de Caracas," for the radioisotopic scans; Blas Bruni Celli, MD, Instituto de Patología, Hospital Vargas – Caracas (Fig. 107); Moisés Guelrud, MD, and José Plaz Abreu, MD, Hospital General del Oeste – Caracas, for the cholangiograms and angiograms; Arturo Michelena, MD, Hospital Central de las Fuerzas Armadas – Caracas (Fig. 87); Diego Núñez h., MD, Hospital Privado "Centro Médico de Caracas," for the CAT scans; Félix Pifano, MD, Instituto de Medicina Tropical – Caracas (Figs. 82 and 83); José Rodríguez Amaya, MD, Hospital General del Oeste – Caracas, for the ultrasound scans.

We are indebted to Mr. Pedro Clotas, Director of Editorial Labor, S.A., and to Paulette Cohen at Alan R. Liss Inc., for their constant interest in publishing this book, as well as to Ann Epner, Eileen Cudlipp, Anne Langlet, and Jeff Brigg who did the yeoman's work of putting the manuscript together.

Pedro J. Grases
Simón Beker G.

CONTENTS

I. INTRODUCTION

I. INTRODUCTION

Two decades ago the clinical work-up of a patient with liver disease was based primarily on physical examination and laboratory tests, some of which were related to liver function. The progress of technology has permitted the incorporation of several methods that allow a more thorough evaluation, not only of function but also of diverse morphological aspects. The advent of laparoscopy, scintigraphy, angiography, manometry, hepatic flow determinations, echography, and computed abdominal tomography and the development of immunological tests, represent unquestionable progress. The availability of percutaneous liver biopsy has also been an invaluable tool when we consider that, before its introduction, the only way to obtain a sample of liver for pathological study was by means of laparotomy. Hence, percutaneous liver biopsy has made feasible not only histological diagnosis but also, in some cases, verification of the etiology. It soon became apparent that a more precise terminology was needed to typify a given case.

The need for a better relationship between the clinician and the pathologist was essential to give sense and permit understanding of the value of the procedure. The physician, including the specialists, became aware that sometimes patients with the same types of clinical manifestations could have different kinds of liver disease, and that liver biopsy could provide the clue for differential diagnosis, indicating appropriate therapy.

The purpose of this book is to offer the clinician a guide that will permit a rational understanding of the method, and to give the pathologist a basis for proper assessment of the true meaning and limitations of the pathological information given to the physician in care. The pathologist must be aware that the interpretation of morphological changes as seen in a liver sample is more valuable when properly correlated with clinical data. What is seen in a liver sample is a minute portion of the organ; the size and integrity of the sample rely in great measure on the ability of the operator and the type of needle used. Sometimes diagnostic terms are imprecise or are used in an etiological context, which is not necessarily appropriate (eg, viral hepatitis). In fact, there are different types of etiological agents with the ability to induce structural changes that are indistinguishable by means of routine microscopic examination.

For practical purposes, most patients with liver disease can be included in one or more of three major groups: those with hepatomegaly, those with jaundice, and those with portal hypertension. In accordance with the findings from other forms of clinical evaluation and laboratory study – that is, to the extent that other variables are introduced – subgroups appear, thus decreasing the diagnostic alternatives.

Later we shall discuss the value of liver biopsy in systemic diseases or diseases of extrahepatic origin with involvement of the liver, and its contribution in following the course of a given disease or evaluating treatment. Finally, we shall briefly analyze the value of surgical biopsy of the liver in the course of a laparatomy.

The reader will easily understand that a book using this approach differs from the ordered presentation of nosological entities that may appear in a conventional textbook. This clinicopathological guide is intended not only for gastroenterologists, hepatologists, internists, and pathologists who are principally the specialists involved with the subject, but also for undergraduate students, interns, and residents, for the purpose of introducing them to this field.

II. NEEDLE BIOPSY TECHNIQUE AND HANDLING OF THE SAMPLE BY THE CLINICIAN

III. PROCESSING OF THE SPECIMEN AND STUDY BY THE PATHOLOGIST

IV. GLOSSARY OF MORPHOLOGIC TERMS

II. NEEDLE BIOPSY TECHNIQUE AND HANDLING OF THE SAMPLE BY THE CLINICIAN

To perform a percutaneous liver biopsy, a needle for coring, suction, or a combination of both is required. The Menghini or disposable needles are the most widely used. In some cases of liver cirrhosis the Vim Silverman needle and the Tru-Cut needle seem to be more appropriate. Materials for local anesthesia and asepsia, plus the selected fixative should be available.

Patients undergoing needle biopsy usually are hospitalized, but the procedure can also be carried out on an outpatient basis if adequate precautions are taken.

It is advisable that the patient be convinced of the need and usefulness of the procedure. If necessary, slight sedation can be achieved with diazepam derivates or phenobarbital.

Intercostal puncture is performed between the anterior and midaxillary lines at the level of maximal dullness. In those patients in which a large nodular hepatomegaly is present, a subcostal approach is used. The patient lies supine in bed with both arms raised, and the following steps are taken:

Local anesthesia of the skin, soft tissues, and liver capsule is achieved. Preliminary perforation of the skin and soft tissues is accomphlished by a special perforator. With the syringe containing a small amount of anesthetic, the Menghini needle is inserted beyond the intercostal during deep sustained inspiration. A small amount of anesthetic is simultaneously injected to clear the needle of any tissue fragments. Upon reaching the liver capsule, the syringe is put on aspiration (negative pressure) and finally is plunged rapidly, full length, into the liver and immediately removed. The liver cylinder, thus obtained is gently expelled into a fixative. The disposable needle may be also used following a similar technique.

The availability of ultrasound and computed abdominal tomography has made guided puncture possible when circumscribed hepatic lesions are detected. We have very little experience with peritoneoscopy-controlled biopsy, but we recognize the advantages in removing tissue under direct observation.

After the biopsy, the patient is advised to remain in bed for several hours. Pulse and blood pressure should be monitored appropriately to detect bleeding. A perenteral analgesic is given if pain is present.

The experienced physician can gain some information by perceiving liver changes when the needle is inserted. He can feel hardness in cases of cirrhosis, fibrosis, or tumors with marked desmoplastic reaction. If a cyst is present, the operator can feel some resistance when the needle penetrates the capsule, followed by a sudden release when it breaks into the lumen.

Once the sample is obtained, gross examination may yield useful information. Changes in the general appearance, color, and external surface may be present.

Macroscopic changes of the sample

General appearance
- Fragmentation (even in hands of an experienced operator) ..... Cirrhosis
- Partial dissolution of the cylinder ..... Necrotic tumor, Abscess wall

Color
- Light yellow ..... Fatty liver
- Light reddish brown ..... Acute viral hepatitis
- Dark reddish brown ..... Passive congestion
- Greenish mottled ..... Cholestasis
- Dark brown or black ..... Dubin-Johnson S. Metastatic melanoma
- Whiteness ..... Neoplasm
- Dark with brown tints ..... Hemochromatosis

Surface
- Nodular or granular ..... Cirrhosis
- Fibrotic bands ..... Fibrosis

Sometimes the sample obtained is inadequate. This can be a result of improper application of the technique (inexperienced operator), the presence of ascites, or when cirrhosis or a necrotic tumor is present.

Contraindications for liver biopsy have been reduced, but they do exist and include the following:

1) Uncooperative patient
2) Disturbances of hemostasis*
3) Diseases near or at the proposed pathway of biopsy (infection of the pleura, lung, subphrenic abscess, or hydatid cyst of the liver)
4) Relative contraindications: marked lung emphysema, marked ascites, lack of liver dullness, severe anemia, and poor general condition

III. PROCESSING OF THE SPECIMEN AND STUDY BY THE PATHOLOGIST

Fixation

Fixation with 10% neutral buffered formaldehyde solution at room temperature for 12–24 hours is adequate. The use of more rapid fixatives (Bouin, Zenker, Dubosq-Brasil) incurs the risk of over-fixation.

Dehydration and paraffin embedding (manual processing)

	Time (minutes)
100% ethanol	15
100% ethanol	15
100% ethanol	15
Benzine	10
Chloroform	10
Xylene	10
Paraffin (58°)	30
Paraffin (58°)	30

*In some cases, replacement of missing coagulation factors can be achieved with fresh-frozen plasma.

Sectioning

Sections are cut on a microtome set at 6–8 μm.

Staining

We routinely use the following special stains, in addition to hematoxylin and eosin (H & E): Masson's trichrome stain (occasionally van Gieson's stain), periodic acid-Schiff (PAS) with and without previous saliva digestion, silver impregnation of reticulin with the Gridley technique, iron staining with Perls' solution. Other special stains are used when indicated: rhodanine stain for copper, orcein stain for HBsAg and copper-associated protein, Congo red for amyloid, Ziehl-Nielsen for acid-fast bacilli, Grocott for fungi, a modified Giemsa for protozoa, etc. Immunoperoxidase techniques for hepatitis B virus (HBV) antigens and alpha-1-antitrypsin have been useful. Their use for liver tissue detection of alphafetoprotein (AFP) and carcinoembryonic antigen (CEA) awaits further experience.

Mounting

The mounting of consecutive sections on several slides allows hepatic morphology study at diverse levels. This will increase the chance of detecting small focal lesions (granulomas, tumors), and in some instances the extent of fibrosis.

Interpretation

In liver pathology we consider the specimen adequate when sections offer useful information even in small samples. This is the case when a small cluster of neoplastic cells is found, an isolated granuloma can be located, or even when a regenerative nodule can be identified. It is advisable to analyze the following factors systematically, and in a given sequence: lobular pattern, arrangement of hepatic trabeculae, parenchyma (hepatocytes), mesenchyma (connective tissue, vessels, and Kupffer cells), and the biliary system. Once the qualitative changes are perceived we quantify the disease, using the terms "slight," "discrete," "moderate," and "marked" or "severe."

Schematic approach to microscopic study of the liver

	Examples of morphological changes
1. Architecture	
1.1. Lobular	Pseudolobules in cirrhosis
1.2. Trabecular	Rosettes in chronic active hepatitis