# Gestational Trophoblastic Disease

# Current Clinical Pathology

Antonio Giordano, Md, Phd

*Series Editor*

For further volumes:
http://www.springer.com/series/7632

Pei Hui
Editor

# Gestational Trophoblastic Disease

## Diagnostic and Molecular Genetic Pathology

Humana Press

*Editor*
Pei Hui, MD, PhD
Department of Pathology
Yale University School of Medicine
New Haven, CT, USA
pei.hui@yale.edu

ISBN 978-1-61779-393-6 e-ISBN 978-1-61779-394-3
DOI 10.1007/978-1-61779-394-3
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2011941658



Printed on acid-free paper

Humana Press is part of Springer Science+Business Media (www.springer.com)

*This book is dedicated to:*

*Professor Bingquan Wu, M.D.*
*An ultimate career mentor and a caring father-in-law*

# Foreword

In placental mammals, the trophoblast plays a critical role in the development of the embryo and fetus, and in normal circumstances is then discarded at the time of parturition, its functions fulfilled. Originating as the outer layer of the developing blastocyst, it ultimately differentiates into a diverse array of morphological phenotypes, each with highly specialized and differing functions: the cytotrophoblast functions as the stem cell component of the villous trophoblast, the syncytiotrophoblast as the terminally differentiated component that is of major importance in maternofetal exchange, and the intermediate trophoblast with multiple functions depending upon its location in villi, in the chorion laeve or in the implantation site. Not surprisingly, in diseases of the trophoblast, the different normal phenotypes are emulated to varying degrees, and the current classification of gestational trophoblastic disease is based on this structure.

In this volume, Dr Hui has brought together a comprehensive overview of gestational trophoblastic disease that includes all the currently recognized entities: complete and partial hydatidiform moles, placental site trophoblastic tumor, epithelioid trophoblastic tumor, gestational choriocarcinoma, persistent gestational trophoblastic neoplasia, placental site nodule, and exaggerated placental site reaction. Each entity is reviewed in detail, with emphasis on genetic background, clinical presentation, pathologic findings and ancillary studies, differential diagnosis, and clinicopathological correlations. Descriptions of the pathology are supported by numerous excellent photomicrographs. Recent advances in our understanding of the genetics of gestational trophoblastic diseases are stressed. Introductory chapters cover the developmental biology of the placenta and the genetic basis of gestational trophoblastic disease, and one chapter is devoted to the molecular diagnosis of gestational trophoblastic disease. This chapter includes a review of the use of short tandem repeat (STR) genotyping, which is of particular value in the diagnosis of hydatidiform moles. The final chapter covers clinical aspects of gestational trophoblastic disease, including treatment. The text throughout is current and thoroughly referenced.

Although written largely by a pathologist, Dr. Hui, with contributions from two other pathologists (Dr. Natalia Buza from Yale and Dr. Katja Gwin from the University of Chicago) and a chapter on clinical aspects of gestational trophoblastic disease by two gynecologists (Dr. Christine Richter and Dr. Peter Schwartz from Yale), this book will be of interest to anyone

involved in the care of patients with gestational trophoblastic disease, including obstetricians and gynecologists as well as pathologists. It can serve as an up-to-date primer and reference source on the classification, clinical features, genetics and molecular diagnosis of gestational trophoblastic diseases, and as an aid to the histopathological diagnosis of these entities. Dr Hui is to be congratulated on making a valuable addition to the literature on these fascinating but complex entities.

New Haven, CT, USA A Brian West, MD, FRC Path

# Preface

Gestational trophoblastic disease (GTD) deserves a special consideration in medicine. It encompasses a group of human disorders of reproduction resulting in significant morbidities in women, and is remarkable for its geographical distributions and varying frequencies in the different age and ethnic groups. In human pathology, these disorders are unique proliferative conditions with regard to their clinical setting, genetic compositions, and varying biological behaviors. Although as one of the earliest recognized human disorders in history, the biology, pathogenesis, diagnosis, and clinical management of the disease are still fascinating many of us either as a diagnostician or as a scientific investigator. My academic interest in GTD incurred at a morning pathology resident conference with Dr. Kurt Benirschke who was visiting Yale in 1997 as a grand rounds speaker. I was presenting him a placental site trophoblastic tumor, a uterine specimen processed by myself and diagnosed by my mentor, Dr. Maria Luisa Carcangiu, a few weeks earlier. Dr. Benirschke challenged me to prove that the lesion was indeed a clonal neoplastic lesion as opposed to a reactive process. His challenge eventually led to my first publication of the X chromosomal requirement by placental site trophoblastic tumor in 2000, and more importantly, opened many fascinating aspects of GTD in my academic career afterward.

With an intended broad spectrum of audience, the book starts with a general review of the medical history, epidemiology, and risk factors for GTD in Chapter 1. Chapter 2 provides a succinct review of developmental aspects of placenta with an emphasis on its early formation and molecular genetic regulation of implantation. Our current understanding of the genetic basis of GTD is given in Chapter 3. The following chapters provide a thorough review of diagnostic histopathology of the each entity of GTD. Although traditional histology is the foundation for morphological recognition, ancillary studies including immunohistochemistry and molecular genotyping have become an integral part of the routine diagnostic algorithm. Each diagnostic entity is richly illustrated histologically, often with multiple examples. Chapter 9 is written to cover the diagnostic entities under the category of persistent trophoblastic neoplasia by the WHO. Invasive mole is primarily discussed here. Chapter 11 provides a thorough review of the emerging molecular diagnostic applications in GTD. Finally, a comprehensive discussion of the clinical presentation and management of GTD is given in Chapter 12.

I can never express enough gratitude to my career mentors, present and past, at Peking University, SUNY at Buffalo, MSKCC and Yale. Their wisdom and training are the major source of knowledge and professional inspirations. Special thanks are owed to many colleagues who shared their insights and/or clinical cases in the past. Finally, this book is a product that represents not only an academic commitment but also the unfettered support and enduring love of my families.

New Haven, CT, USA Pei Hui, MD, PhD

# Contents


**1 Gestational Trophoblastic Disease: General Aspects** ..... 1
Pei Hui

**2 Developmental Biology of the Placenta** ..... 15
Pei Hui

**3 Genetic Basis of Gestational Trophoblastic Disease** ..... 41
Pei Hui

**4 Complete Hydatidiform Mole** ..... 57
Pei Hui

**5 Partial Hydatidiform Mole** ..... 77
Natalia Buza

**6 Placental Site Trophoblastic Tumor** ..... 91
Pei Hui

**7 Epithelioid Trophoblastic Tumor** ..... 105
Katja Gwin

**8 Gestational Choriocarcinoma** ..... 127
Pei Hui

**9 Persistent Trophoblastic Neoplasia** ..... 139
Pei Hui

**10 Tumor-Like Trophoblastic Conditions** ..... 147
Pei Hui

**11 Molecular Diagnosis of Gestational Trophoblastic Disease** ..... 161
Pei Hui

**12 Clinical Aspects of Gestational Trophoblastic Disease** ..... 179
Christine E. Richter and Peter E. Schwartz

**Appendix** ..... 195

**Index** ..... 201

# Contributors

**Natalia Buza, MD** Department of Pathology, Yale University School of Medicine, 310 Cedar Street, PO Box 208023, New Haven, CT 06520-8023, USA
natalia.buza@yale.edu

**Katja Gwin, MD, PhD** Department of Pathology, University of Chicago Medical Center, 5841 S. Maryland Ave (MC6101), Chicago, IL 60637, USA
Katja.Gwin@uchospitals.edu

**Pei Hui, MD, PhD** Department of Pathology, Yale University School of Medicine, 310 Cedar Street, 254B New Haven, CT 06520-8023, USA
pei.hui@yale.edu

**Christine E. Richter, MD** Division of Gynecologic Oncology, Department of Obstetrics, Gynecology & Reproductive Sciences, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA
christine.richter@yale.edu

**Peter E. Schwartz, MD** Division of Gynecologic Oncology, Department of Obstetrics, Gynecology & Reproductive Sciences, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA
peter.schwartz@yale.edu