

HUGH ZACHARIAE

SKIN HISTAMINE

*Spectrofluorometric Studies on Normal
and Diseased Skin*



MUNKSGAARD COPENHAGEN 1965

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Denne afhandling er i forbindelse med omstående tidligere publicerede
afhandlinger af det lægevidenskabelige fakultet ved Københavns
universitet antaget til offentlig at forsvares for den
medicinske doktorgrad.

København, den 19. maj 1965.

Harald Gormsen

h. a. dec.

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Previous Publications

- I. H. Zachariae: Skin histamine in urticaria pigmentosa. Spectrofluorometric assay. *Acta dermat.-venereol.* 1963, **43** : 125.
- II. H. Zachariae: Skin histamine in urticaria. A spectrofluorometric assay. *Acta dermat.-venereol.* 1963, **43** : 214.
- III. H. Zachariae: Histamine in human skin. A spectrofluorometric assay. *Acta dermat.-venereol.* 1964, **44** : 219.
- IV. H. Zachariae: Skin histamine in erythema multiforme exudativum. *Acta dermat.-venereol.* 1964, **44** : 261.
- V. H. Zachariae: Influence of betamethasone, a synthetic steroid, on histamine in human skin. A spectrofluorometric assay. *Acta dermat.-venereol.* 1964, **44** : 330.
- VI. H. Zachariae: Polymyxin B, a potent releaser of histamine in human skin. *Acta dermat.-venereol.* 1964, **44** : 338.
- VII. H. Zachariae: Histamine in delayed skin reactions. Fluorometric determinations on patch tests. *J. invest. Derm.* 1964, **42** : 431.
- VIII. H. Zachariae: Histamine and mast cells in fetal skin. *Proc. Soc. exp. Biol.* 1964, **117** : 63.
- IX. H. Zachariae: Histamine in a transplantable mouse mastocytoma. *Proc. Soc. exp. Biol.* 1964, **117** : 283.
- X. A. Marckmann & H. Zachariae: Histamine in full thickness skin autografts of rat. *Proc. Soc. exp. Biol.* 1964, **117** : 705.
- XI. A. Marckmann & H. Zachariae: Histamine and mast cells in full thickness skin grafts of pig. *Acta chir. scand.* 1965, **129** : 12.
- XII. H. Wulff, H. Zachariae & K. Øhlenschläger: The leukocytic response to aseptic inflammation in urticaria pigmentosa. *J. invest. Derm.* 1965, **44** : 381.

Preface

This survey of histamine in skin is based on a series of investigations carried out during the period 1962 to 1964 at the Connective Tissue Research Laboratory, Department of Skin and Venereal Diseases and at the Central Laboratory, Department of Clinical Chemistry, Rigshospital, University of Copenhagen.

My deepest thanks are due to professor *G. Asboe-Hansen*, M. D., director of the Connective Tissue Laboratory and head of the Department of Skin and Venereal Diseases, Rigshospital for his deep interest, constant encouragement and valuable criticism as well as for the complete scientific freedom I enjoyed.

I wish also to thank professor *P. Astrup*, M. D., head of the Department of Clinical Chemistry, for most excellent working conditions.

The experiments on pigs reported in one of the publications were performed at the Institute for Experimental Research in Surgery, University of Copenhagen. It is a pleasure to thank director *H. H. Wandall*, M. D. for the permission to undertake this investigation.

I am indebted to dr. *Thomas Laursen* and chemist *Johannes Christiansen* for their valuable assistance, interest and kind advice. My sincere thanks is extended to professor *E. Husfeldt*, M. D., professor *E. Husted*, M. D., *Henning Andersen*, M. D., *Helge Andersen*, M. D., *Ragna Rask-Nielsen*, Ph. D., *M. Pers*, M. D., *S. Ulrich*, M. D., *Niels Lomholt*, M. D., and *Lis Zachariae*, M. D. for providing a great many of the specimens used in these studies. My special thanks are due to dr. *A. Marckmann*, dr. *H. R. Wulff* and dr. *Kirsten Øhlenschläger* for their stimulating collaboration in some of my studies. To Mr. *M. Nyholm*, M. A., I am grateful for valuable help and guidance in the statistical calculations.

For able and careful technical assistance during the experimental work and the preparation of the manuscript I thank Miss *Annelise Christensen*, Mrs. *Nina Christiansen*, Mrs. *Birgit Thorsen*, Miss *Kirsten Hasløv*, Mrs. *Wanda Juncker*, laboratory technicians, Miss *Wibeke Larsen*, medical student, Miss *Edith Andersen*, Miss *Lis Munk*, nurses, and Miss *Julie Leifeldt*, secretary. My thanks go also to Mr. *John Winther*, who prepared all photographs.

The studies were aided by grants from Mr. & Mrs. *Reinholdt W. Jorck's* Foundation, *F. L. Smidth & Co.'s* Foundation, *Johann* and *Hanne Weimann*, née *Seedorff's* Foundation, "Fonden til Lægevidenskabens Fremme" to dr. *A. Marckmann*, and USPHS Grant AM 06209-02 to dr. *G. Asboe-Hansen*.

Through her constant encouragement, unselfish support and great practical assistance, my wife, dr. *Eva Zachariae*, has a large share in these studies. I am gratefull to her and my children for their patience and resignation during the years of this work.

Fredensborg, April 1965.

Hugh Zachariae

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Introduction

Shortly after *Windaus & Vogt* in 1907 had synthesized histamine, the marked pharmacological effects of this chemical substance were discovered. In the following decade, histamine was shown to be present in most animal tissues, including skin. This fact led to research into the question of the physiological role of histamine, a problem which has not yet been solved. The relationship between histamine and allergy has been dealt with for years. Although an analogy between the pharmacological effects of histamine and those of anaphylaxis was pointed out by *Dale & Laidlaw* as early as 1910, histamine has not yet been proved responsible for the clinical manifestations in allergic conditions. The role played by histamine as an edema producing substance in connection with skin changes of various types in man has been made the subject of many authors. Few, however, have measured histamine. Histamine research until now has been carried out mainly on animals.

Previously the only suitable means of measuring histamine in tissues was bioassay (*Barsoum & Gaddum* 1935, *Code* 1937). The concept of the importance of histamine in human pathology, however, stimulated the search for increasingly sensitive methods (*Lubschez* 1950, *Lowry, Graham, Harris, Priebat, Marks & Bregman* 1954).

The spectrofluorometric assay (*Shore, Burkhalter & Cohn* 1959) has made possible the measurement of histamine in small skin biopsies. It was natural, therefore, to investigate the levels of skin histamine in normal and diseased skin. The present experiments were undertaken in an attempt to elucidate the significance of changes in skin histamine and to afford a survey of the role of histamine in skin.

