

Second
Edition

Nasal Allergy

Niels Mygind

Foreword by A.W. Frankland

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Foreword

It might be agreed that in the field of allergy, the nose represents only one small area of a vast field of interest. Should a book be written on such a subject? Any book written to clarify our ideas must serve a useful purpose, since doctors often have very little precise knowledge of the sensitivity, specificity and predictive value of the tests they order or use. The value of complicated techniques in education and research is indisputable but for clinical purposes these tests are often informative but seldom essential. This concise and readable book enables clinicians to familiarize themselves with every possible aspect of the allergic nose.

We seem to advance slowly, since in Britain we have been celebrating the centenary of Blackley's book on seasonal hay fever. In it he described how he carried out provocation tests on the skin, eye, nose and chest. His work and his book were forgotten. This present book on nasal allergy will remain an invaluable guide to all interested in the allergic nose and certainly will be the authoritative work on the subject.

A. W. FRANKLAND
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Introduction

To first edition

In the long series of excellent textbooks dealing with the immune system and allergic disease, nasal allergy is usually described as a postscript to the clinically more significant disease, bronchial asthma. ENT textbooks usually describe nasal allergy as an introduction to the principal chapter dealing with surgical treatment. In both cases allergic nasal disease is reduced to a disorder of secondary importance, and in some respects it is. But nasal allergy is common. In a recent study 15 per cent of medical students had clinical hay fever and an additional 9 per cent had a positive pollen skin test without clinical symptoms. Considering the many textbooks dealing with the immune system, bronchial asthma and nasal surgery, it is the author's opinion that the allergic nose deserves a textbook of its own.

In preparing such a book, the author has been guided by two basic purposes. The first has been to prepare a practical clinical guide for the care of rhinitis patients, and the second has been to review the basic principles that underlie our understanding of allergy and nasal disease.

An attempt has been made to bring together the structural, physiological, immunological and therapeutic aspects of nasal allergy. Within such a broad field the reader's knowledge of the subject will vary from chapter to chapter. To make the text comprehensible for as many readers as possible, it has been necessary to include topics of the most elementary kind. Therefore, some chapters contain truisms for the immunologist, while they may be difficult to read for the rhinologist and vice versa. When a chapter deals with an aspect of no particular interest to the reader, a glance at the figures and summary may be adequate for progression. In this way it is hoped that the book will prove readable for the student and may provide, also, the senior clinician and scientist with some new data.

To second edition

Although reports on progress in allergy research appear in quick succession, the reader may wonder why a second edition of this textbook is produced less than one year after the first. The recent introduction of a new drug for nasal use, ipratropium, is the explanation. This compound has proved useful in the management of rhinitis, and therefore a chapter was added to the text. For practical reasons the new Chapter 24 has not been indexed. Only minor corrections have been made in other chapters.

Acknowledgements

This textbook is obviously not the result of one man's work. It is based mainly on a series of investigations carried out in collaboration with colleagues, to whom the author is indebted for permission to use the original results. The accomplishment of these investigations has been made possible by the positive attitude of the Heads of the Department of Otolaryngology, Rigshospitalet, and help from the technicians at the Otopathological Laboratory. Figures and micrographs have been prepared with skill and enthusiasm by the Department of Medical Photography, Rigshospitalet. Of decisive importance has been the effort of Dr Louis A. Phillips and H.G. Mygind, my father, who have acted as the editorial staff. Also Mrs Linda Bishop and Mrs Francis Weinstein have been most helpful.

Each chapter has been read by a specialist in Scandinavia, England or the U.S.A. The names of these specialists, mentioned below, are no guarantee of the quality of the text, but it has been improved considerably by their comments and suggestions.

Finally all chapters have been read by Dr A.W. Frankland, Director of the Allergy Department, St Mary's Hospital, London.

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Abbreviations

ACTH	adrenocorticotrophic hormone
ATP	adenosine triphosphate
ATP-ase	adenosine triphosphatase
Bdp	beclomethasone dipropionate
c-AMP	cyclic adenosine monophosphate
c-GMP	cyclic guanosine monophosphate
cyclic AMP	cyclic adenosine monophosphate
cyclic GMP	cyclic guanosine monophosphate
DNA	deoxyribonucleic acid
DSCG	sodium cromoglycate
ECF-A	eosinophil chemotactic factor of anaphylaxis
ECF-C	eosinophil chemotactic factor of complement
ENT	ear, nose, throat
FEV ₁	forced expiratory volume in one second
HPA axis	hypothalamo-pituitary-adrenal axis
IgA	immunoglobulin A
IgD	immunoglobulin D
IgE	immunoglobulin E
IgG	immunoglobulin G
IgM	immunoglobulin M
LDH	lactic dehydrogenase
MW	molecular weight
ppm	parts per million
RAST	radioallergosorbent test
RIST	radioimmunosorbent test
RNA	ribonucleic acid
SCG	sodium cromoglycate
SRS-A	slow-reacting substance of anaphylaxis

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PART I

ULTRASTRUCTURE

Structure and ultrastructure of the nose

Macroscopic anatomy of the nasal cavity

Epithelium

Basement membrane

Lamina propria

Connective tissue cells

Connective tissue fibrils

Ground substance—tissue fluid

Mast cells

Eosinophil leucocytes

Neutrophil leucocytes

Lymphocytes

Plasma cells

Lamina propria *continued*

Macrophages

Blood vessels

Glands

Anterior serous glands

Small seromucous glands

Secretion

Macroscopic appearance

Mucin

Electrolytes

Proteins

Nerves

Summary

Patients with allergic nasal diseases are treated either by an ENT surgeon (principally interested in the nose; structure and surgery) or by an allergist (principally interested in the immune system, allergy diagnosis and immunotherapy). However, knowledge both of the nose and of the immune system is necessary for optimal clinical and scientific work with these patients. Therefore, the first three chapters of this book deal with the anatomy and function of the nose (mainly written for the allergist) and with the immune system (mainly written for the ENT surgeon).

Macroscopic anatomy of the nasal cavity

In *fetal life* the primitive nasal cavity (developed from ectoderm) is separated by the bucco-nasal membrane from the rhinopharynx (developed from endoderm). In the sixth fetal week this membrane breaks and the primitive nasal cavity and the rhinopharynx are then connected. Later the nasal cavity is separated from the oral cavity by the soft and hard palates (Johnston *et al.* 1958). Both processes can be incomplete and give rise to congenital deformities (choanal atresia, cleft palate) which impair the function of the nose.

On the lateral wall of the nasal cavity are formed three folds and these develop into the three turbinates (conchae). Lateral growth of epithelial cords from the nasal cavity occur and these form the paranasal sinuses. The ethmoidal, sphenoidal, maxillary and frontal sinuses develop during childhood into air-filled cavities, which are completed in the adult.

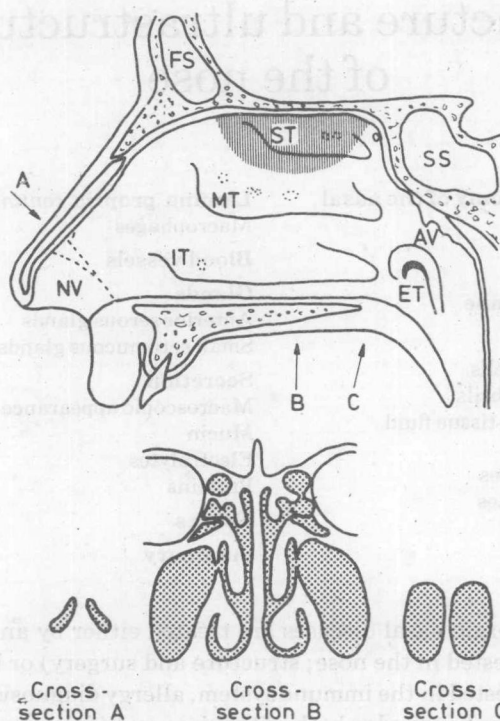


Fig. 1.1. Lateral wall of the nasal cavity in $\frac{2}{3}$ the natural size, and cross-sections through (A) the internal ostium, (B) the middle of the nasal cavity and (C) the choanae. Hatched area in the upper figure: olfactory region.

NV: Nasal vestibule. IT: Inferior turbinate and orifice of the nasolacrimal duct.

MT: Middle turbinate and orifices of frontal sinus, anterior ethmoidal sinuses and maxillary sinus, mentioned in antero-posterior direction. ST: Superior turbinate and orifices of posterior ethmoidal sinuses. Behind the superior turbinate: the orifice of the sphenoidal sinus. FS: Frontal sinus. SS: Sphenoidal sinus. AV: Adenoid vegetations. ET: Orifice of eustachian tube.

In *adults* the anterior $\frac{1}{3}$ of the nasal cavity is surrounded by the cartilage and the bone structure of the outer nose. There is considerable individual and racial variation. General conclusions about the nasal cavity and its functions cannot be drawn from the appearance of the outer nose, but individuals with high narrow noses may have increased tendency to nasal stenosis.

The nasal cavity is subdivided into right and left halves by the nasal septum. These two halves open to the face through the anterior nasal apertures (nares, *nostrils*), and communicate behind with the rhinopharynx via the posterior nasal apertures (*choanae*) (Fig. 1.1). In Danish men the distance from the tip of the nose to the pharyngeal wall averages 11 cm

(Andersen *et al.* 1971). Total surface area of both nasal cavities is about 150 cm² and total volume about 15 ml.

Each half of the nasal cavity can be subdivided into three parts, namely the nasal vestibule, the olfactory region and the respiratory region.

The nasal *vestibule* is limited above and behind by the internal ostium (limen nasi, valve area) (Fig. 1.1). A curved elevation lateral to the ostium corresponds to the lower margin of the upper lateral cartilage which can be felt as a sharp prominence with the finger some 1.5 cm from the nostril. The *internal ostium* of the nose plays an important role in nasal functions as it is the narrowest place in the cavity, the cross-section approximating only 0.3 cm² on each side (Masing 1967; Proctor *et al.* 1973). A cross-section of the nose shows that the nasal cavity, due to the turbinates, is not a wide tube, but a 1–5 mm slit especially narrow in the upper part (Fig. 1.1).

The *olfactory region* of about 10 cm² (compared to 170 cm² in the German shepherd dog) is localized to the superior turbinate and the opposed part of the septum.

The *respiratory region* comprises the rest of the cavity.

Shrinking the mucosa with ephedrine, applied by spray or tampon, is often necessary in order to improve the view obtained by *rhinoscopy*. The lateral wall is dominated by the large *inferior turbinate* just above the nasal floor. Deeper in the nasal cavity (about half-way) is the *middle turbinate* which hangs like a polyp. Finally, even further back in the nose is the, rarely visible, *superior turbinate*. The nasal cavity lateral to the turbinates is named the inferior, middle and superior meatuses.

Structures not visible on such an examination (Fig. 1.1) include the inferior meatus, which is hidden by the tip of the inferior turbinate and the orifice of the nasolacrimal duct, located just posterior to this tip. Similarly, the orifices of the frontal, maxillary and anterior ethmoidal sinuses, located in the middle meatus, are hidden from view. The diameter of these orifices approximates 2–6 mm. The nasal septum is seldom positioned exactly in the midline. Septal deviations, septal spurs and septal crusts may partially obstruct the nasal airways unilaterally or bilaterally.

Epithelium

In the *respiratory region* the mucosa consists of an epithelium resting on a basement membrane and a lamina propria ('submucosa') (Fig. 1.9). In the posterior $\frac{2}{3}$ of the nasal cavity the mucosa is covered by pseudostratified columnar epithelium, in which most of the cells are ciliated. Varying epithelial types are found in the anterior $\frac{1}{3}$ (from the skin in the vestibule to a vertical line, one centimetre posterior to the front edge of the inferior turbinate). In an antero-posterior direction the epithelial types are:

- 1 Squamous epithelium (Fig. 1.2a).



Fig. 1.2. Scanning electron micrographs, showing different epithelial surfaces in the anterior (a), middle (b) and posterior (c) part of the anterior third of the nasal cavity. (a) Squamous epithelium without actual microvilli ($\times 1,100$). From Mygind and Bretlau (1974b). By courtesy of *Acta allergologica*.

- 2 Transitional epithelium (a stratified epithelium with cuboidal surface cells covered by microvilli) (Fig. 1.2b).
- 3 Pseudostratified columnar epithelium, in which only a few cells are ciliated (Fig. 1.2c).

In the paranasal sinuses the epithelium is either a thin ciliated columnar epithelium or of the simple columnar ciliated type with a few goblet cells and gland openings (Messerklinger 1958).

The typical *respiratory epithelium* (ciliated columnar pseudostratified) consists of four dominant cell types, ciliated columnar cells, non-ciliated columnar cells, goblet cells and basal cells (Fig. 1.3). The ratio of columnar to goblet cells is about 5:1. All cells rest on the basement membrane, but the

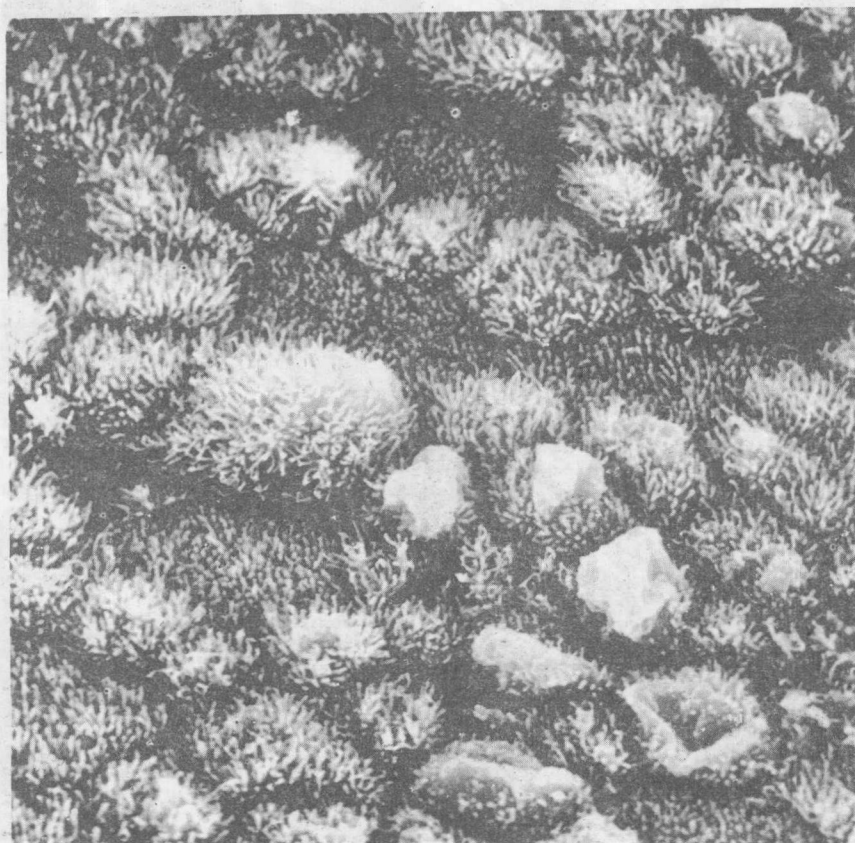


Fig. 1.2 (cont.)

(b) Non-ciliated pseudostratified or transitional epithelium. All cells are covered by 300-400 thin microvilli ($\times 3,000$).

basal cells do not reach the luminal surface. They are primitive cells from which the columnar and the goblet cells develop.

Columnar epithelial cells are often, but not always, covered by *cilia*. These ciliated cells contain several mitochondria, most of which cluster in the apical part of the cell. Mitochondria are the chief energy source of the cell and are necessary for the considerable working capacity of cilia. Development of cilia (ciliogenesis) takes place after replication and transformation of the cell centrioles to basal bodies. Cilia originate from basal bodies which also serve to anchor them to the cell.

Cilia are long, thin, mobile projections from the luminal surface of the cell. The characteristics of a cross-section is a ring of nine doublet microtubules surrounding two single central microtubules, the detailed structures