INTERNATIONAL REVIEW OF

Experimental Pathology

VOLUME 19—1979

G. W. RICHTER

EDITED BY

M. A. EPSTEIN

INTERNATIONAL REVIEW OF

Experimental Pathology

G. W. RICHTER

University of Rochester
School of Medicine and Dentistry
Rochester, New York

EDITED BY

M. A. EPSTEIN

University of Bristol
Medical School
Bristol, England

VOLUME 19—1979

ACADEMIC PRESS
NEW YORK · SAN FRANCISCO LONDON
A Subsidiary of Harcourt Brace Jovanovich, Publishers

COPYRIGHT © 1979, BY ACADEMIC PRESS, INC.
ALL RIGHTS RESERVED.
NO PART OF THIS PUBLICATION MAY BE REPRODUCED OR TRANSMITTED IN ANY FORM OR BY ANY MEANS, ELECTRONIC OR MECHANICAL, INCLUDING PHOTOCOPY, RECORDING, OR ANY INFORMATION STORAGE AND RETRIEVAL SYSTEM, WITHOUT PERMISSION IN WRITING FROM THE PUBLISHER.

ACADEMIC PRESS, INC.
111 Fifth Avenue, New York, New York 10003

United Kingdom Edition published by
ACADEMIC PRESS, INC. (LONDON) LTD.
24/28 Oval Road, London NW1 7DX

LIBRARY OF CONGRESS CATALOG CARD NUMBER: 62-21145

ISBN 0-12-364919-6

PRINTED IN THE UNITED STATES OF AMERICA
79 80 81 82 9 8 7 6 5 4 3 2 1

Contributors

Numbers in parentheses indicate the pages on which the authors' contributions begin.

BJÖRN AFZELIUS, *Wenner-Gren Institute, University of Stockholm, Stockholm, Sweden (1)*

MONIQUE DUBOIS-DALCQ, *National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20014 (101)*

C. J. ELSON, *Immunobiology Group, Department of Pathology, University of Bristol, Bristol, England (137)*

Y. KOCH, *Department of Hormone Research, The Weizmann Institute of Science, Rehovot, Israel (45)*

J. D. NAYSMITH, *Immunobiology Group, Department of Pathology, University of Bristol, Bristol, England (137)*

E. OKON, *Department of Pathology, Hadassah University Hospital, Jerusalem, Israel (45)*

CHARLES A. SANTOS-BUCH, *Department of Pathology, Cornell University Medical College, New York, New York 10021 (63)*

R. B. TAYLOR, *Immunobiology Group, Department of Pathology, University of Bristol, Bristol, England (137)*

Contents

此为试读,需要完整PDF请访问: www.ertongbook.com

Pathology of Measles Virus Infection of the Nervous System: Comparison with Multiple Sclerosis

MONIQUE DUBOIS-DALCQ

B-Cell Tolerance and Autoimmunity

C. J. ELSON, J. D. NAYSMITH, AND R. B. TAYLOR

INTERNATIONAL REVIEW OF EXPERIMENTAL PATHOLOGY, VOL. 19

The Immotile-Cilia Syndrome and Other Ciliary Diseases

BJÖRN A. AFZELIUS

Wenner-Gren Institute, University of Stockholm, Stockholm, Sweden

Copyright © 1979 by Academic Press, Inc.
All rights of reproduction in any form reserved.
ISBN 0-12-364919-6

I. Introduction

One of the cornerstones in pathology is the concept of cellular pathology formulated by Rudolf Virchow more than 120 years ago. It is based on the insight that cells are the unit of life and states that diseases are due to a malfunctioning of the cells. With present-day knowledge, many examples of such malfunctionings can be given and further defined in biochemical terms and in the language of molecular biology. It is, however, fairly rare that a disease can be traced to malfunctionings of a certain organelle, that is, to a cell component specialized for one or several functions. Apart from Luft's disease, which affects the mitochondrial size and coupling (Luft *et al.*, 1962; Di Mauro *et al.*, 1976), some lysosomal diseases (De Duve, 1975; Hers, 1963; Hers and van Hoof, 1973), and the peroxisomal diseases, hypocatalasia and acatalasia, no disorders have been described which can be regarded as cell organelle diseases. It is the purpose of this review to present evidence for a disorder which is believed to be caused by defective cilia and to review some data on the occurrence of abnormal cilia, evidently formed in response to environmental insults.

The question thus raised is: Are there pathological conditions which are caused by a malfunctioning of cilia and of all cilia wherever they occur in the body? It will be shown that the question can be answered in the affirmative, and that evidence can be given for an "immotile-cilia syndrome." This is an "organelle disease" in the sense that it affects the same organelle in every cell in which that organelle occurs. It is thus a generalized disorder rather than one which affects a certain organ in the body. During the investigation of this syndrome, I have been surprised to find that no generalized ciliary disease has ever been described nor, apparently, has even been searched for. The concepts of Virchow are not being kept alive in the minds of modern pathologists.

II. The Cilium

A. Definition

A cilium can be defined as an extension of the cell with an appearance resembling the scheme in Fig. 1. It is thus a machinery consisting of nine microtubular doublets in a ring around two central microtubules and provided with an enveloping extension of the cell membrane, usually called the ciliary membrane.

The nine microtubular doublets have protrusions, extending from one side toward the neighboring doublet; these are called the *dynein arms*. There are also less prominent connections between the doublets, the thin connect-

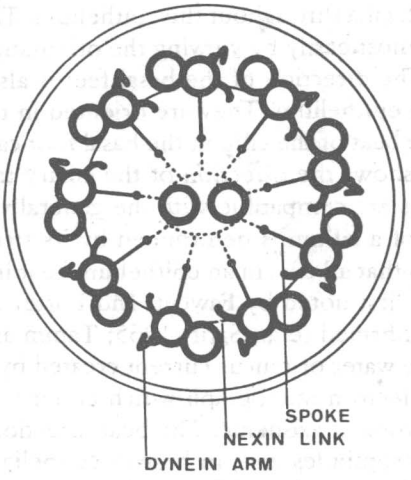

FIG. 1. Diagram of the cross-section of a cilium or of the central part of a sperm tail. Nine microtubular doublets surround two central microtubules and are in turn surrounded by the ciliary membrane. There are three kinds of connections between the microtubules: the dynein arms, the nexin links, and the spokes. The dynein arms provide the motor force during the ciliary bendings.

ing *nexin links.* The two central filaments are surrounded by semicircular rib-like structures, the *central sheath.* Between the central sheath and the peripheral doublets are slender radial threads, which are called *spokes* (or sometimes tautologically, *radial spokes*). The complex of microtubular doublets and singlets, associated dynein arms, central sheath, nexin links, and spokes is called the *axoneme.*

At the base of the cilium there is a *basal body,* or *kinetosome,* which is similar to a centriole and in some cells indeed may be derived from one. Basal bodies vary structurally more than the axoneme. Those in human ciliated epithelia usually have both a *basal foot* and a short *ciliary rootlet.* The basal foot projects from the basal body parallel to the cell surface and the ciliary rootlet extends toward the interior of the cell. Both these projections may have a striated appearance and, to some degree, they resemble collagen fibers.

The width of a cilium is 0.2 μm. Its length varies in different tissues, but in human ciliated epithelia is about 6 μm.

For the purpose of this presentation, three regular features (Gibbons, 1961a,b) of the normal ciliated epithelium have to be kept in mind: (a) The dynein arms all go in the same direction; they have a clockwise direction when seen from the inside of the cell toward the tip of the cilium. (b) The orientation of the 9 + 2 microtubules is the same to within 30° in neighbor-

ing, and also distant, cilia throughout the epithelium. The orientation of this complex is judged most easily by viewing the orientation of the two central microtubules. (c) The direction of the basal feet is also constant to within 30° throughout the epithelium. They are oriented in the same direction as that of the effective beat of the cilium; the basal foot can hence be regarded as an arrow which shows the direction of the ciliary transport.

These regularities are compatible with the generally held viewpoint that the beat direction of a cilium is determined by its structural organization, and with the notion that all cilia in an epithelium beat in the same direction. This regularity was first noted by Fawcett and Porter (1954) and has since been repeatedly confirmed (e.g., Satir, 1965; Tamm and Horridge, 1970). The direction of the water or mucus current created by the cilia can directly be deduced in an electron micrograph which either includes the basal feet or else shows the crosscut axoneme. The beat direction is perpendicular to the central two microtubules and, in human epithelia, may be toward the microtubular doublets, numbered 5 and 6.

B. Chemical Basis of Ciliary Action

A few words have to be said about the chemical composition of the cilium. The two main components are *tubulin* and *dynein,* which make up the microtubules and the dynein arms, respectively. There is a functional analogy between the tubulin–dynein system in cilia and the actin–myosin system in muscles (or of most other contractile systems in nonmuscular cells). Thus, the dynein arms are structures which are instrumental in the sliding of microtubules during ciliary work, as are myosin filaments during muscle contraction. Like myosin, the dynein molecule has a high molecular weight and is an ATPase.

The microtubule sliding hypothesis for cilia was first proposed by Afzelius (1959). Satir (1965) and Gibbons (1975) gave direct evidence for the validity of this hypothesis. The dynein arms can thus be considered to provide the motor force for beating of cilia.

The nexin links presumably are responsible for the maintenance of axoneme structure during sliding (Stephens, 1970). They seem to limit the sliding by being stretchable only to a certain degree. It has also been suggested that the nexin links pull the doublets together in the initial phase of bend induction, allowing the dynein arms to interact with adjacent doublets (Summers, 1975).

The spokes may interact with the central sheath at the start of bending (Warner and Satir, 1974) as a part of the mechanism for converting sliding into bending. It also appears probable that the spokes give the cilium a certain rigidity, preventing it from making sharp nicks, while allowing it to bend.

The genes for the proteins making up these structures can be assumed to be chromosomal. A suggestion has been made that the basal body may carry its own DNA, which participates in some parts of the morphogenesis (Randall, 1959), but proof for this suggestion is lacking. So is proof for the proposal that genes for ciliary material are cytoplasmic, contain RNA, and act by means of a reverse transcriptase (Went, 1977a,b).

Although the biochemistry and functional anatomy of cilia are known in detail, the events during ciliary movements are largely unknown. There is much uncertainty in many of the concepts summarized in the above paragraphs.

III. Human Ciliated Structures

A. Distribution in the Human Body

Ciliated epithelia are seen in the following places in the human body:

1. The *upper airways*, which include the nasal passages (Jahnke, 1972; Mygind and Bretlau, 1973; Okuda and Kanda, 1973), the paranasal sinuses (Friedmann and Bird, 1971), the eustachian tubes (Harada, 1977), and the pharynx down to the orifice of the esophagus.

2. The *lower airways*, which include the trachea (Pavelka *et al.*, 1976; Rhodin, 1966), the primary and secondary bronchi (Konradova, 1968; Konradova *et al.*, 1975), and the bronchioles down to the respiratory bronchioles.

3. The mucosa of the *middle ear* (Hilding and Heywood, 1971; Kawabata and Paparella, 1969).

4. The *ependymal lining* of the brain and the central canal of the spinal cord (Dempsey and Nielsen, 1976; Worthington and Cathcart, 1963).

5. The *ductuli efferentes* on the border between the testis and the epididymis (Holstein, 1969; Morita, 1966).

6. The endometrial lining of the deeper parts of the cervix and the *oviducts* including their fimbriae (Clyman, 1966; Fadel *et al.*, 1976; Fredricsson and Björkman, 1962; Ludwig *et al.*, 1972; More and Masterton, 1976; Nilsson and Nygren, 1972).

The total area covered by ciliated epithelia may amount to 150 cm^2 in the turbinates and nasal passages and to about 300 cm^2 in the paranasal sinuses (Proctor, 1964). The ciliated area of the trachea and lungs can be estimated to be around 5000 cm^2 (or 0.5 m^2). Other ciliated regions are comparatively small. With a density of six cilia per μm^2, the total number of cilia in ciliated tissues of the human body is of the order of 3×10^{12}.

Ciliated structures also exist elsewhere in the human body; the above list is not exhaustive. Isolated cilia or cilia-like structures may also be found in various locations:

此为试读,需要完整PDF请访问: www.ertongbook.com

7. *Spermatozoa.* The human sperm tail can be regarded as a modified cilium or flagellum. In a cross-section, the end-piece of the sperm tail is indistinguishable from a cilium. In the principal piece of the tail, a wrapping called the *fibrous sheath* is interposed between the axoneme and the enclosing cell membrane. There are also nine *coarse fibers* associated with the nine axonemal doublets. These fibers are thick in the sperm middle-piece and taper posteriorly. The shortest coarse fibers are those which are associated with the two "lateral" doublets (termed Nos. 3 and 8). They are replaced posteriorly by laminae, which connect these two doublets with the fibrous sheath. The coarse fibers associated with doublets termed Nos. 1, 5, and 6 are the thickest and longest ones (Pedersen, 1972).

The axoneme extends from the distal centriole at the base of the head toward the tip of the tail. Its total length is 45 μm, of which the anterior-most, 4- to 5-μm-long region is surrounded by mitochondria and called the middle-piece, and the posterior-most, 1- to 7-μm-long region is called the end-piece. It is evident that the sperm tail contains tubulin, dynein, and the other ciliary proteins, but it also contains others not present in ordinary cilia.

8. *Sensory cells.* Some sensory cells carry what is called a sensory hair or sensory cilium on their free surface. Thus, olfactory cells have 6–20 olfactory cilia that extend from an apical, protruding hillock. In their proximal, 2-μm-long portion these cilia have the conventional axoneme pattern, except that in mammals dynein arms are missing (Menco, 1977). In their distal, prolonged portion the cilia have two or a few simple microtubules. The basal feet are usually directed toward the center of the protruding hillock.

The hair cells of the vestibular organ each carry a group of stereocilia (a misnomer for a prominent, stiff microvillus) and a single, 40-μm-long cilium, here called kinocilium (Flock and Duvall, 1965; Engström *et al.*, 1972). Even though the kinocilium is usually stiff and rigid, it can display continuous motility (Flock *et al.*, 1977).

Hair cells in the organ of Corti resemble those of the vestibular organ, except that the kinocilium is constantly present only in fetal and early postnatal life and is usually missing in adult animals (Bredberg *et al.*, 1972).

9. *Other tissue cells.* It has been a surprise to many investigators to find a single cilium on cells in which the presence of cilia had not been expected. Thus, single cilia have been found in ganglion cells in the brain (Allen, 1965), pineal gland (Barnes, 1961), adrenal gland (Wheatley, 1967), pancreas (Boquist, 1968), liver (Wheatley, 1968), kidney (Flood and Totland, 1977; Latta *et al.*, 1961; Pfaller and Klima, 1976), heart (Myklebust *et al.*, 1977), cartilage (Scherft and Daems, 1967), connective tissue (Kubota *et al.*, 1975), dermis and epidermis (Daróczy and Feldmann, 1974), and many other organs. The above examples refer to both animal and human tissues. The single cilia usually lack the two central microtubules and thus have an

axoneme of the 9 + 0 type, although there are some which are of the 9 + 2 type with dynein arms (Chung and Keefer, 1976).

10. *Embryonic tissues.* Solitary cilia are particularly common on embryonic epithelia. According to Fonte *et al.* (1971) both those cells which are undergoing rapid cell division but have not yet attained an "adult stage" of differentiation and those which have attained an adult stage of differentiation carry solitary cilia. Thus, the 10-day-old mouse fetus has single cilia projecting into the lumen of the neural tube (Seinsch, 1976), the lumen of the esophagus (Ševčenko and Vacek, 1973), and presumably in cells of most other tissues. According to Rash *et al.* (1969) cilia may be present at some time in virtually all embryonic tissues, regardless of derivation. These cilia usually are of the 9 + 0 type but occasionally are of a 9 + 2 type with dynein arms (Kapa *et al.*, 1976).

B. Presumed Functions

Ciliated structures in the 10 different locations listed above cannot be expected to have the same function. The mucosa of the upper and lower airways and the middle ear has columnar ciliated lining cells and mucus-secreting glands. Goblet cells in the lining secrete mucin (a viscous polysaccharide-protein); the glands contain cells that secrete either mucoid or serous material (Proctor, 1964). A mucous blanket covers the lining cells. It is two layered, with an inner stratum in which the cilia beat and an outer layer that is acted upon by the cilia and in fixed preparations can be preserved as a finely fibrillar network. Each stratum is maximally 5 μm wide. Occasionally, myelin figures can be seen in the inner layer; these are thought to be remnants of a surfactant which gives the inner layer a low viscosity (Yoneda, 1976). The outer layer forms a viscous blanket which may trap inspired particles and is carried along by the drag of the cilia (and to a minor degree by swallowing, by coughing, and by airflow). Another role of the outer layer is to protect the inner layer and the cilia from desiccation. Calculations have shown that the movement of the mucous blanket depends critically on the viscosity and depth of either the outer mucous or the inner serous layer (Blake, 1975; Ross, 1971).

Each cilium beats with a frequency of 20 beats per second and goes on beating throughout the cell life (Huberman *et al.*, 1977). The tip of the cilium has a maximal speed exceeding 30 mm/minute. Another way to express this is to claim that the tip of the cilium travels 300 m a week. The rate of flow of the mucous blanket is less, owing to its viscosity. In the nose, it is 4–6 mm/minute (Hilding, 1932).

This type of ciliary action is called a *mucociliary transport* and, because its role is to trap and remove foreign or other unwanted particles, its effect is called a *clearance.* The direction of the mucociliary transport of the upper

airways is backward and downward; that of the lower respiratory tract is upward. In both cases the direction of the flow is toward the orifice of the esophagus. The airways are thus cleared of bacteria, viruses, and dust particles which are swept away by the cilia and disposed of in the stomach. The physiology of the upper airways has been reviewed by Proctor (1977).

There is also a clearance of the middle ear toward the eustachian tube (Sade, 1967) and of the eustachian tube toward the nasopharynx (Rogers *et al.*, 1962).

The ependymal epithelium has ciliated cells but no goblet cells. It is thus capable of a clearing action (Cathcart and Worthington, 1964) but not of a mucociliary clearance. The cilia evidently create water currents which are shaped so that the entire ependymal surface is being swept clear and the blind ependymal pockets have fluid circulating through them. It is presumed that large amounts of cellular debris can be cleared from the ependymal surface. The role of cilia in the brain and spinal cord is thus to keep the fluid in constant movement and to remove any cellular debris before it has a chance to accumulate. Direct observations of the ciliary motion have been made on material removed from human brains at autopsies (Worthington and Cathcart, 1963), and experiments on laboratory animals have also demonstrated a clearing action (Cathcart and Worthington, 1964; Nakayama and Kohno, 1974).

On the other hand, there are no direct observations on the ciliary activity of the ductuli efferentes of the testis. There are no goblet cells in these ductules (Holstein, 1969). It is presumed that ciliary beats help propel spermatozoa and fluid toward the epididymis.

The situation in the oviduct is slightly more complex. This mucosa is a mixture of nonciliated secretory cells and ciliated cells. The secretion may be a nutritive mucoprotein. The ciliary currents may be toward the uterine or ovarian end depending on species and region of the oviduct (Gaddum-Rosse and Blandau, 1976). In the human oviduct the cilia beat toward the uterus. Measured frequencies of the ciliary beat in rabbits depend on stages of the estrus cycle and on previous copulation (Borell *et al.*, 1957). Possibly, these measurements reflect changes of the mucous layer rather than in the ciliated cells. It is believed that the ciliary activity serves as a mechanism for egg transport (Halbert *et al.*, 1976), but the oviducts also have muscular activity. The oviduct mucosa in birds has the same appearance as that in mammals, and the cilia cannot possibly be expected to exert any influence on the transport of bird eggs (Sandoz and Boisvieux-Ulrich, 1976).

The connection between sperm motility and fertilization capacity is also unsettled. It is often believed that the spermatozoon has to swim actively in order to reach the site of fertilization. This is not quite true, as spermatozoa introduced into the oviduct will be passively transported to the neighborhood of the egg. However, motility is probably a necessary quality for at

least the rat sperm cells to go through the valve between the uterus and oviduct (Leonard and Perlman, 1949), and presumably their motility will aid in dispersing the cumulus cells surrounding the oocyte. It has also been suggested that sperm motility may be a signal to the oocyte that a healthy spermatozoon is approaching (Afzelius, 1970).

Whether the sensory cilia have to be actively motile for proper functioning has not been open to experimentation and there are no data in the literature on this matter. Olfactory cilia in amphibians have an active motility (Menco, 1977; Reese, 1965), but no data on motility of their mammalian counterparts have been presented.

The existence of single cilia on cells of compact tissues has been puzzling to the investigators and functions other than motility have usually been given. These cilia are called primary, solitary, isolated, residual, vestigial, or immature cilia, and they are so jammed into the narrow interstices of the tissue that they cannot possibly beat. It has therefore been suggested that the single cilia function as sensory hairs detecting chemical or mechanical stresses (Allen, 1965). Another suggestion states that differentiating cells are deprived of their ability to divide by a transformation of the mitotic centrioles into a ciliary basal body (Fonte *et al.*, 1971; Rash *et al.*, 1969). The cell usually has a pair of centrioles, and only one of them is associated with a cilium (Barnes, 1961). The various types of kidney cells provided with a solitary cilium are exceptional in this respect, as they project into a wide tubular lumen. It has been suggested that these cilia are capable of motility (Pfaller and Klima, 1976) and may serve to create turbulence and prevent laminar flow of the tubular fluid (Latta *et al.*, 1961), but these suggestions are not plausible, as shown by Flood and Totland (1977).

The last group of cilia—those of embryonic epithelia—belongs to the least studied group, and the only suggestions for its significance is the idea presented above: by a transformation of the mitotic centriole into a ciliary basal body, further mitotic divisions are prevented.

C. Accessibility to Investigations

Before progressing further, it is practical to consider which types of cilia—from the 10 groups discussed in the sections above—are accessible to examination either with the light or the electron microscope, and what other measurements of ciliary activity can be made.

By far the easiest material to obtain for study is semen. The only limitation is that only men in certain age groups can be examined.

It is relatively easy to get a scraping from the nasal mucosa or to get ciliated epithelia during removal of polyps. Similarly, biopsies from the endometrial mucosa can be obtained without trauma during a gynecological examination and studied in the living state. One is less likely to find ciliated

cells in endometrial biopsies than in nasal biopsies prepared for electron microscopy.

Other ciliated mucosae are less amenable to examination by electron microscopy. A biopsy from the bronchial tree requires operation under general anesthesia. Mucosa from the maxillary sinus can be removed for study by a Luc–Caldwell operation (Toremalm *et al.*, 1975). Similarly, mucosa from the inner ear can be available in connection with ear operations. It is sometimes feasible to take specimens from a deceased person, as the cilia have been shown to beat up to 36 hours after death (Hilding, 1957).

Even if biopsies from the airways cannot be easily obtained (except from the nasal mucosa), measurements of the mucociliary clearance can be performed on epithelia *in situ*. For this puspose, the test subject is asked to inhale a radioactively tagged test aerosol and external measurements of the radioactivity of the lung are made at regular intervals over a period of 2 or more hours. Different methods for production and use of test aerosols have been reviewed by Camner (1971). Alternative methods for demonstration of the mucociliary activities include a direct observation of visible particles deposited in the nose (Ewert, 1965; Hilding, 1932) and in the trachea (Santa Cruz *et al.*, 1974), or application of small saccharin particles to the nose followed by measurement of the time until the sweet taste of saccharin is felt in the pharyngeal region (Andersen *et al.*, 1974).

IV. The Immotile-Cilia Syndrome

A. Ultrastructural Considerations and Clearance

A syndrome has recently been described which is characterized by congenitally nonfunctioning cilia (Afzelius, 1976; Eliasson *et al.*, 1977; Mossberg *et al.*, 1978). This "immotile-cilia syndrome" seems to provide the investigator with the keys to questions about the role of ciliary motility in the human body.

The first step in unraveling of the immotile-cilia syndrome was the discovery by Pedersen and Rebbe (1975) of a case having immotile spermatozoa, devoid of the dynein arms. The deficiency provides a perfectly satisfactory explanation of the sperm immotility and makes it unnecessary, and even misleading, to refer to the semen sample—as has later been done—as a case of necrospermia, that is of dead spermatozoa.

A little later, two similar cases were investigated in Stockholm. These were brothers attending a fertility clinic and their spermatozoa were found to have straight and immotile tails, lacking dynein arms (Afzelius *et al.*, 1975). Examination of the vital staining properties of the ejaculate and of its

oxygen consumption and lactic acid production showed the percentage of living spermatozoa to be normal.

It was natural to pose the question of whether cilia other than sperm tails were also affected. For this reason the hospital records were studied. Both men were recorded as having suffered since early childhood from chronic expectoration of mucoid and purulent sputum. Both had a history of chronic and recurrent infections in the upper and lower airways. This certainly indicates an inadequate mucociliary mechanism.

A logical step at this stage was to investigate all further cases that could be obtained from the fertility clinic records and which had the characteristics of living but completely immotile spermatozoa. Two such cases were examined with respect to the mucociliary transport in the tracheobronchial tract (Camner *et al.*, 1975). Both were shown to have an extremely slow, probably absent, transport. The material was then extended to six men and one woman (Eliasson *et al.*, 1977), and later to fourteen cases (Mossberg *et al.*, 1978), and again the mucociliary transport was found to be significantly reduced. During the 2 hours of measurement, only 8% (on the average) of the inhaled, radioactively tagged test particles were removed from the tracheobronchial tract, compared with a measured average of 62% for 63 healthy subjects, studied by the same technique (Mossberg *et al.*, 1978). Another way to express these values is that the percentage retention after 2 hours is 92 ± 8% (SD) for persons suffering from the immotile-cilia syndrome and 38 ± 22% in healthy nonsmokers or exsmokers. This striking difference presents the first proof that men with living but immotile spermatozoa also have immotile cilia.

Other proofs were required and obtained thanks to the cooperation of the examined people, many of whom volunteered to have a biopsy taken either from the turbinate area of the nasal mucosa or from a bronchus. Some biopsies were suspended in balanced salt solutions and examined in the living state. No ciliary activity was displayed. The biopsy samples were also processed for an electron microscopical investigation, and the following observations were made: (1) dynein arms were either lacking or greatly reduced in number. In some cases there were short projections rather than normal-sized dynein arms; (2) the orientation of the cilia was random rather than fixed; (3) the orientation of the basal foot on the basal body was also random rather than fixed (Figs. 2–9). These features are interpreted to mean either that the cilia cannot move (most likely), or else that the cilia have some motility but beat in all directions rather than cooperatively toward the pharynx.

Parallel to these investigations, Pedersen and Mygind (1976) have examined the cilia from the nasal mucosa of a woman with daily airway symptoms consisting of a cough and a purulent secretion from the respiratory tract. The cilia were found to be devoid of dynein arms, and mucociliary clearance

此为试读,需要完整PDF请访问: www.ertongbook.com