ATYPICAL CILIA IN HUMAN ENDOMETRIUM

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Motile cilia throughout the bios possess a constant number of fibrils which are arranged in a regular and consistent pattern. Yet, during a study on the fine morphological changes of human uterine epithelium in different phases of the cycle, we observed an impressive number of cilia showing a wide variety of structural anomalies previously unreported in a mammalian tissue. Such a conspicuous deviation from the normal may be relevant for an evaluation of the function of the ciliated cells of the human endometrium.

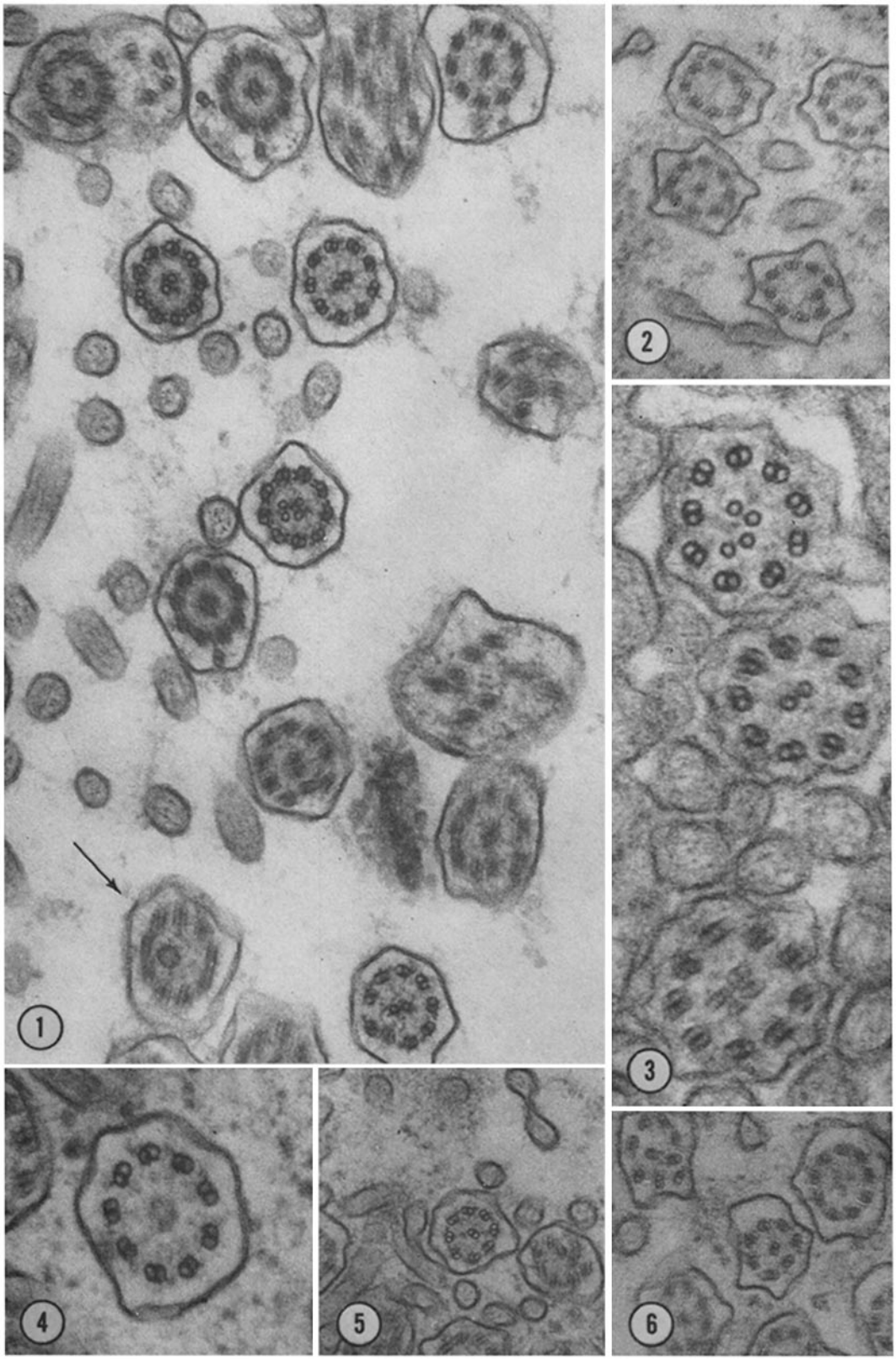
The study was performed on 17 endometrial biopsies obtained from 15 patients in reproductive age at different stages of the menstrual cycle. The patients were seen for minor gynecological affections, none of which included abnormal uterine bleeding or endometritis. Two patients were biopsied twice in the course of our study. Fragments of endometrium, obtained randomly from the uterine cavity by the suction method, were immediately diced into small blocks which were fixed in 1% OsO_4 with salts added (17), or in 2.5% glutaraldehyde in 0.1 M cacodylate buffer (12). Glutaraldehyde fixation was followed by postosmication of the tissue. Embedding was performed in Epon 812 (8). The thin sections were stained with lead hydroxide (6) and studied with Hitachi HU 11A and HU 11C electron microscopes.

Anomalous cilia were found in 10 of 15 patients, and their presence could not be related to any particular stage of the cycle. One of the patients was biopsied twice during the same cycle and showed cilia abnormalities in both tissue samples. In the positive cases, the structural defects were present in a large number of cells, where they often involved the majority of cilia (Fig. 8). Anomalies were found in the shaft of the cilium as well as in the apical cytoplasm of the ciliated cells.

A detailed description of the wide variety of defects observed in the ciliary shafts would be beyond the scope of this report. In essence the defects were represented by the following: (*a*) aberrations of the number of elements of the axial complex, which were of the plus type (Figs. 1 and 3) or of the minus type (Figs. 2, 4–6); (*b*) abnormal arrangement of the fibrils of the axial complex (Figs. 1, 8, and 12); and (*c*) abnormal structural characteristics of the fibrils of the axial complex (Fig. 1).

Two or more anomalies were occasionally found in the same ciliary shaft. Fig. 7, for example, illustrates a minus defect of the peripheral elements and a plus aberration of the central fibrils. Plus and minus aberrations were frequently associated with dislocation of the fibrils (Figs. 1–3 and 7).

Giant shafts containing multiple (Figs. 13, 17, and 18) and often variously oriented sets of filaments (Fig. 15) were frequently observed. Another anomaly was the erratic pattern of filament termination at the tips (Figs. 9–11), which was inconsistent also with that described by Satir in normal motile cilia (14).



The structural anomalies observed in the apical cytoplasm of the ciliated cells were the presence of aberrant ciliary filaments (Figs. 14 and 16) and the long insertion of the cilia into the cytoplasm, with persistence of the central fibrils (Fig. 16).

Although the occurrence of anomalous cilia has been reported by previous investigators (1, 3, 9, 11, 13), the example of a single type of cell characterized by a variety of ciliary defects such as those described in this study is unprecedented. The finding of aberrant cilia in 10 of 15 endometrial biopsies indicates that the incidence of structural defects in the ciliated cells of the human endometrium is very high. It is probable that the number of anomalous cilia in this tissue is even higher than that shown in our study, since our observations were based on an accidental finding and did not derive from a systematic study of ciliated cells of the uterine epithelium. The high incidence of the structural defects becomes even more apparent if one considers that the number of ciliated cells in the human endometrium is low, relative to the total cell population (16). We must conclude, thus, that aberrant cilia are not an unusual feature of human uterine epithelium.

The questions whether these anomalies occur with a similar frequence in other types of human ciliated epithelia and whether the incidence of these anomalies in man is higher than in other species obviously cannot be answered in a definite way at the present time. It would seem, however, that the ciliated cells of the endometrium represent an exception since defects similar for incidence and variety to those described here have not been reported in other human ciliated epithelia (4, 10). Typical of the human endometrium is that its cell population becomes totally renewed at each cycle. Thus, it is possible that the numerous aberrant cilia observed in this study are related to the rapid periodic process of cell renewal. This possibility must be given serious consideration, particularly in view of the study by Roth and Shigenaka (11) who also observed abnormal patterns during ciliary morphogenesis. Against this possibility, however, militate the results of studies made on other tissues during rapid cell regeneration; regeneration of hepatic tissue after hepatectomy, for example, is normally accompanied by swift reconstitution of normal cell components (7) and, even more pertinent, posttraumatic regeneration of tracheal epithelium was seen to be associated with *de novo* formation of typical cilia (2).

Notwithstanding the occasional finding of a few anomalous cilia (1, 3, 9, 11, 13), the universality of the 9 + 2 pattern in the axial complex of motile cilia and flagella has been sufficiently demonstrated (see reference 15 for review); also the importance of this pattern for ciliary function has been demonstrated (5). Satir (13) rightly stated that the occasional occurrence of atypical cilia reinforces the concept that the 9 + 2 pattern represents an evolutionary stabilization, because it provides functional advantages over other patterns. Thus, the presence of frequent anomalies in the sparse ciliated cells of the human endometrium could also indicate that either these cells or their cilia represent evolutionary vestigia devoid of any important function.

This study was supported by a Ford Foundation Grant in Reproductive Biology.

Received for publication 6 May 1968, and in revised form 11 July 1968.

FIGURE 1 Numerical (plus type) and geographical aberrations of the fibrils of the axial complex. In the cilium marked by the arrow, the central elements have been substituted by a single tubular structure. × 49,000.

FIGURE 2 Two 9 + 0 cilia with dislocation of one peripheral doublet. × 47,000.

FIGURE 3 Two 9 + 4 cilia. × 103,000.

FIGURE 4 9 + 0 cilium far from tip. × 94,000.

FIGURE 5 8 + 2 cilium far from tip. × 43,000.

FIGURE 6 7 + 2 cilium far from tip. × 47,000.

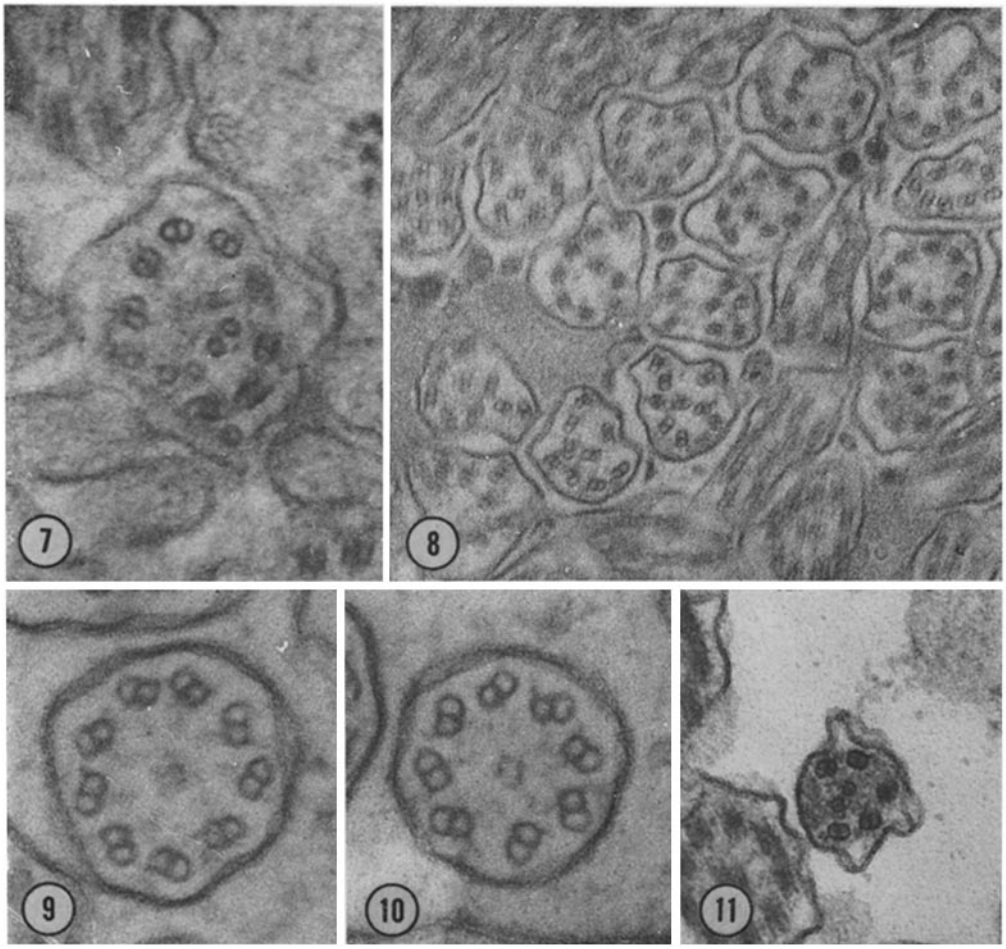


FIGURE 7 Cilium with eight peripheral doublets and six dislocated singlets. × 123,000.

FIGURE 8 Numerical and geographical aberrations in the majority of cilia from a single cell. × 54,000.

FIGURES 9–11 Erratic patterns of fibril termination at tips of cilia. Fig. 9, × 122,000; Fig. 10, × 122,000; Fig. 11, × 72,500.

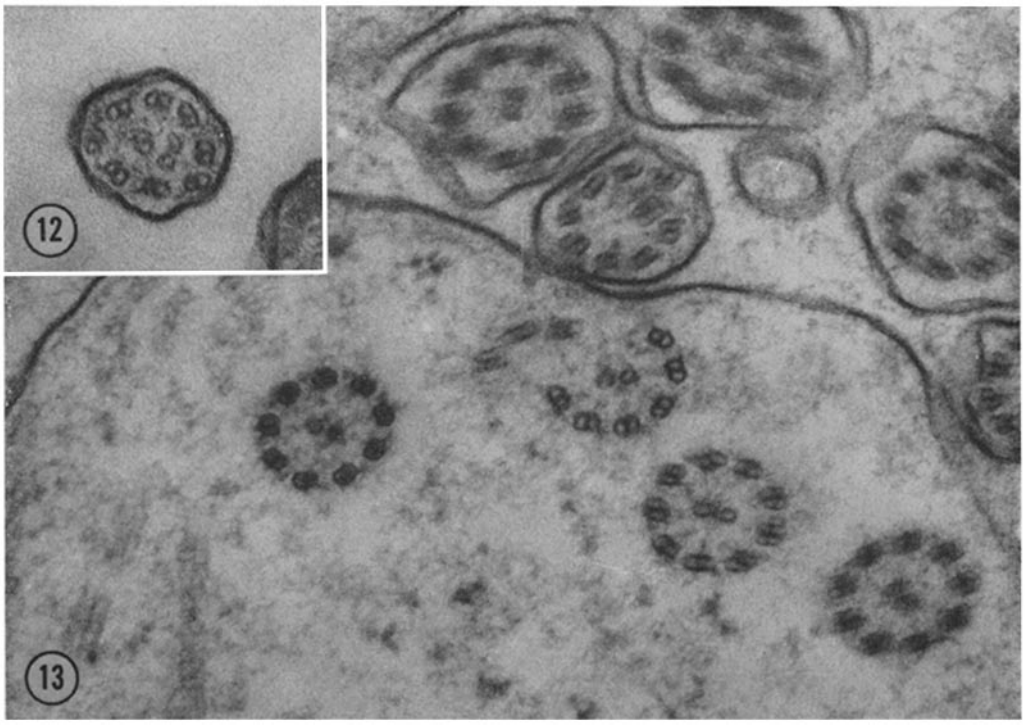


FIGURE 12 9 + 2 cilium with one doublet in central position. × 75,000.

FIGURE 13 Giant cilium with four 9 + 2 axial filaments, one of which shows dislocation of three peripheral doublets. × 84,500.

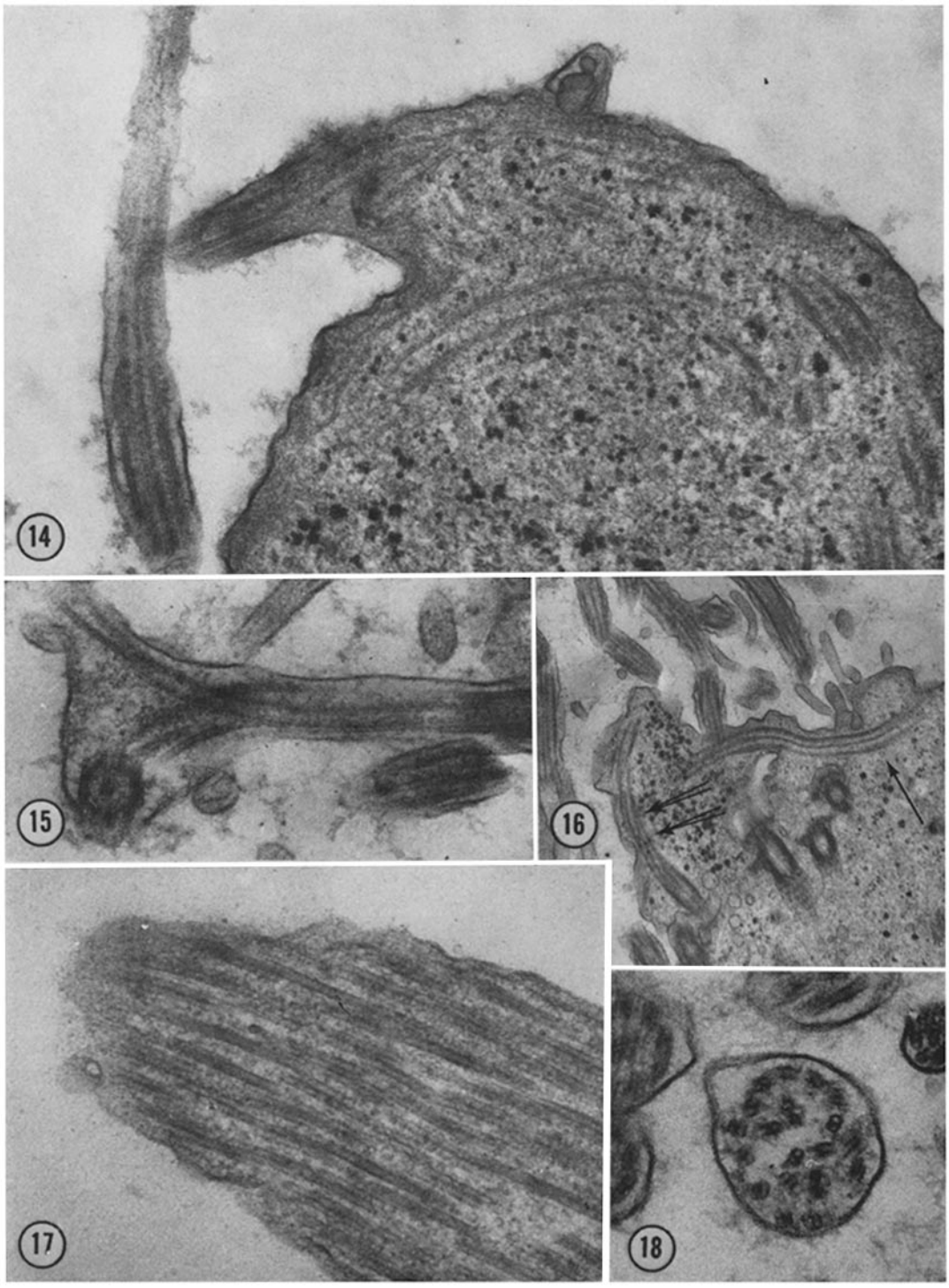


FIGURE 14 Aberrant elements of the axial complex in the apical cytoplasm of a ciliated cell. × 37,000.

FIGURE 15 Differently oriented axial complexes in a single shaft. × 35,000.

FIGURE 16 Aberrant cilium in the apical cell cytoplasm (arrow) and long insertion of cilium with persistence of central fibrils in the basal body (double-stemmed arrows). × 17,500.

FIGURES 17 and 18 Giant cilia in longitudinal (Fig. 17) and transverse section (Fig. 18). Fig. 17, × 64,500; Fig. 18, × 50,500.

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