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ABSTRACT BOOK

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12. IMMOTILE CILIA SYNDROME - ULTRASTRUCTURAL AND IMMUNOGENETIC ANALYSIS IN THREE FAMILIES.

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Immotile cilia syndrome (ICS) is a congenital disease due to a disorder of the ciliar movements. ICS is part of a larger group of primary dyscinesias (Rossman et al., 1984). The worst cases show a complete absence of ciliar motion due to: a-partial or complete loss of internal or external dinein bridges (Afzelius 1976, Howel et al., 1980), b-absence or anomalies of the radial spokes (Sturgess et al., 1979), c-loss of central microtubuli (Howel et al., 1980), d-transposition of an external couple of tubules (Sturgess et al., 1980). In less advanced cases ciliar activity may be only partially impaired due to lack or excess of single microtubuli or couples (Antonelli et al., 1983, Rossman et al., 1984). Recently (Niggerman et al., 1992, Afzelius et al., 1991) cases have been described in which the disfunction was not linked to ultrastructural changes in the microtubuli but to their greater lenght. The Authors describe three couples of sibling with ICS, taken from three non related families. Diagnosis was done through clinical symptoms, radiologic findings and both ultrastructural and immunogenetic examination. One couple showed pulmonary chronic disease while in the other two only upper airway infections where evident. Analisis by Electron Microscopy of nasal mucosa biopsies revealed structural anomalies of the cilia, characterized by isolated single microtubuli and couples of tubuli arranged abnormally in the assonema. HLA study of all members of the three families showed significant association between ICS and HLA-DR7- and aplotype DQW2, common in all siblings with the disease ($p=0.0099$, $RR=25.94$). Studies specifically oriented to establish a relationship between the different kinds of ciliar malfunction and specific biochimical and genetic abnormalities ar still scarse today (Cagnon et al. 1982). ICS comprises a clinicaly not homogeneous entity deriving probably from a range of different underlying genetic diseases. The involved genes may be located on several different chromosomes. Mutations in only one gene may perhaps be the cause of an abnormal ultrastructure and its deriving ciliar malfunc-

tion. The gene for the beta-tubulin has been located on Chromosom 6 in the segment 6p21-6pter (Floyd-Smith et al. 1985). This is also the area were the HLA genes are located. For the examined cases our results support the hypothesis of a primary disease of the beta-tubulina due to mutation or its abnormal expression due to influences from the nearby HLA genes. The described cases of supranummerary tubules may be due to excess production of tubulin or excess transport. It can be suggested that the disease may be given by a rare mutation of a gene of the tubulin or of the genes of a carrier protein, in linkage disequilibrium with the haplotype HLA-DR7; DQW2 in the persons of our study.