Polycystic kidney disease--the ciliary connection

Albert C M Ong, Denys N Wheatley

Lancet 2003; 361: 774-76

Sheffield Kidney Institute, Division of Clinical Sciences (North), University of Sheffield, Sheffield S5 7AU, UK (A C M Ong DM); and Department of Cell Pathology, University of Aberdeen, Aberdeen, UK (D N Wheatley PhD)

Correspondence to: Dr A C M Ong (e-mail: a.ong@sheffield.ac.uk)

Context “Cystic degeneration” of the kidneys was first described pathologically in 1841 and "polycystic kidneys" as a clinical syndrome in 1888. The heritable nature in some families was noted in 1899, and autosomal dominant and recessive patterns of inheritance of polycystic kidney disease (PKD) were later recognised. Autosomal dominant PKD is one of the most common human genetic diseases and results from mutations in PKD1 or PKD2. These genes encode two proteins, polycystin-1 and polycystin-2.

Starting point Primary cilia are cellular organelles previously thought by some to be vestigial. New findings from several species, including algae, nematodes, and mice, implicate defects in structure or function of primary cilia as a possible common mechanism central to the development of some forms of recessive PKD. Two recent reports propose a causal link between ciliary dysfunction and autosomal dominant PKD. B Yoder and colleagues (J Am Soc Nephrol 2002; 13: 2508-16) show that polycystin-1 and polycystin-2 are localised to primary cilia in cultured renal epithelial cells. S Nauli and colleagues (Nat Genet 2003; 33: 129-37) show that polycystin-1 and polycystin-2 function as flow-sensitive mechanosensors in the same signal-transduction pathway.

Where next? Cystic epithelial cells show many altered cellular properties, including changes in proliferation, apoptosis, adhesion, differentiation, polarity, extracellular matrix synthesis, and fluid transport. The next important steps in PKD research will be to define the physiological roles of primary renal cilia and how defects in ciliary structure and function lead to the development of a cystic phenotype in different forms of PKD.