FURTHER READING

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section 21 Disorders of the kidney and urinary tract 4986 be made with some confidence, although the evidence base for bene- ficial intervention at lower levels of albuminuria is not secure. Current recommendations from national diabetes associations advise at least annual screening, based on the diagnostic flowchart shown in Fig. 21.10.1.3. Extrapolating the known effects of ACE inhibitors on a re- duction of UAER to a possible prevention of severe albuminuria and thus endstage renal disease has led several authors to propose a poten- tial cost benefit from the early use of these agents. However, there are no consistent data showing a benefit of these drugs in terms of pre- vention of moderately increased albuminuria in normoalbuminuric patients with normal or well-controlled blood pressures. Can glycaemic control reverse established nephropathy? The DCCT was inconclusive, but data from clinic populations and following pancreas transplantation suggest benefit, at least in type 1 diabetes. The situation in type 2 is much less certain. Why does intensive glycaemic control fail to completely prevent development of moderately increased albuminuria? Glycaemia is one of many factors leading to nephropathy, so correc- tion of this alone may not be enough. Moreover, even in the DCCT complete glycaemic normalization was not achieved. It is possible that newer insulins and delivery systems with continuous glucose monitoring may make sustained normoglycaemia more easily achievable and enable us to test its effectiveness. Do drugs that block the renin–angiotensin system prevent or only delay the development of nephropathy? Can they reverse established nephropathy? The data are not conclusive, partly because of the relatively short duration of many trials, but most studies show a benefit in terms of reduction of UAER. For those with severely elevated albuminuria and CKD stage 3 and beyond, there is no doubt that renin–angiotensin system blocking drugs delay endstage renal disease. For moderately increased albu- minuria, there are no studies of sufficient power to confirm benefit on hard clinical endpoints such as mortality or endstage renal dis- ease. Primary prevention of moderately increased albuminuria using renin–angiotensin system blockade has only been shown in hypertensive type 2 patients or those at high cardiovascular risk. Likely developments in the near future Hyperglycaemia is thought to lead to nephropathy through sev- eral pathways, as outlined in Box 21.10.1.1. There are develop- ments in most of these fields, with the following being studied in trials: pyridoxamine and other inhibitors of glycation; atrasentan and other endothelin inhibitors; allopurinol; antifibrotic agents; al- dosterone antagonists; and inhibitors of inflammatory pathways. FURTHER READING ACCORD Study Group (2008). Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med, 358, 2545–59. ACCORD Study Group (2010). Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med, 362, 1575–85. Adler AI, et al. (2003). Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Study (UKPDS 64). Kidney Int, 63, 225–32. American Diabetes Association.

(2015). Executive summary: stand- ards of medical care in diabetes—2015. Diabetes Care, 38 Suppl 1, S4. Bilous R (2008). Microvascular disease: what does the UKPDS tell us about diabetic nephropathy? Diabetic Med, 25 Suppl 2, 25–9. Bilous R, et al. (2009). Effect of candesartan on microalbuminuria and albumin excretion rate in diabetes: 3 randomised trials. Ann Intern Med, 151, 11–20. DCCT/EDIC Research Group (2003). Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progres- sion of diabetic nephropathy. JAMA, 290, 2159–67. 0.1% (0.0% to 0.1%) 0.1% (0.1% to 0.2%) 2.0% (1.9% to 2.2%) 1.4% (1.3% to 1.5%) 3.0% (2.6% to 3.4%) 4.6% (3.6% to 5.7%) D E A T H 19.2% (14.0% to 24.4%) 2.8% (2.5% to 3.2%) 2.3% (1.5% to 3.0%) No nephropathy Microalbuminuria Macroalbuminuria Elevated plasma creatinine or renal replacement therapy 0.3% (0.1% to 0.4%) Fig. 21.10.1.4 Annual transition rates and 95% confidence interval through stages of nephropathy in 5097 newly diagnosed type 2 diabetic patients in the UKPDS.

 4987 DCCT/EDIC Research Group (2011). Intensive diabetes therapy and glomerular filtration rate in type 1 diabetes. N Engl J Med, 365, 2366–76. Diabetes Control and Complications Trial Research Group (1993). The effect of intensive treatment of diabetes on the development and progression of long term complications in insulin dependent dia- betes mellitus. N Engl J Med, 329, 977–86. Finne P, et al. (2005). Incidence of end stage renal disease in patients with type 1 diabetes. JAMA, 294, 1782–7. Forbes JM, Cooper ME (2013). Mechanisms of diabetic complications. Physiol Rev, 93, 137–88. Fullerton B, et al. (2014). Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus. Cochrane Database Syst Rev, 2, CD009122. Gaede P, et al. (2008). Effect of multifactorial interventions on mor- tality in type 2 diabetes. N Engl J Med, 358, 580–91. Gaston RS, et al. (2004). Transplantation in the diabetic patient with advanced chronic kidney disease: a task force report. Am J Kidney Dis, 44, 529–42. He F, et al. (2002). Diabetic retinopathy in predicting diabetic neph- ropathy in patients with type 2 diabetes and renal disease: a meta- analysis. Diabetologia, 56, 457–66. Hellemons ME, et al. (2012) Validity of biomarkers predicting onset or progression of nephropathy in patients with type 2 diabetes: a sys- tematic review. Diabetic Med, 29, 567–77. Hemmingsen B, et al. (2011). Intensive glycaemic control for patients with type 2 diabetes: systematic review with meta-analysis and trial sequential analysis of randomised clinical trials. BMJ, 343, d6898. Hovind P, et al. (2004). Predictors for the development of microalbuminuria and macroalbuminuria in patients with type 1 diabetes mellitus: inception cohort study. BMJ, 328, 1105–8. International Diabetes Federation (2017). Diabetes atlas, 8th edition. https://diabetesatlas.org JBS3 Board (2014). Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). Heart, 100, ii1–i67. Kato M, et al. (2014). Diabetic nephropathy—emerging epigenetic mechanisms. Nat Rev Nephrol, 10, 517–30. Kidney Disease Outcomes Quality Initiative (2012). KDOQI Clinical Practice Guidelines for diabetes and chronic kidney disease: 2012 update. Am J Kid Dis, 60, 850–86. Mahmoodi BK, et al. (2012). Associations of kidney disease measures with mortality and endstage renal disease with and without hyper- tension: a meta-analysis. Lancet, 380, 1649–61. Mann JF, et al. (2009). Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet, 372, 547–53. Marshall SM, Flyvbjerg A (2006). Prevention and early detection of vascular complications of diabetes. BMJ, 333, 475–80. Mauer M, et al. (2009). Renal and retinal effects of enalapril and losartan in type 1 diabetes. N Engl J Med, 361, 40–51. Molitch ME, et al. (2004). Nephropathy in diabetes. Diabetes Care, 27 Suppl 1, S79–83. Mooyaart AL, et al. (2011). Genetic associations in diabetic nephrop- athy: a meta-analysis. Diabetologia, 54, 544–53. Olsen S, Mogensen CE (1996). How often is NIDDM complicated with non-diabetic renal disease? An analysis of renal biopsies and

the lit- erature. Diabetologia, 39, 1638–45. Orchard TJ, et al. (2010). In the absence of renal disease, 20 year mor- tality risk in type 1 diabetes is comparable to that in the general population: a report from the Pittsburgh epidemiology of diabetes complications study. Diabetologia, 53, 2312–19. Palmer SC, et al (2015). Comparative safety and efficacy of blood pressure lowering agents in adults with diabetic kidney disease: a net- work meta-analysis. Lancet, 385, 2047–56. Parving H-H, et al. (2012). Cardiorenal end points in a Trial of Aliskiren for type 2 diabetes. N Engl J Med, 367, 2204–13. Pavkov ME, et al. (2006). Increasing incidence of proteinuria and declining incidence of end stage renal disease in diabetic Pima Indians. Kidney Int, 70, 1840–6. Robertson LM, Waugh N, Robertson A (2006). Protein restriction for diabetic renal disease. Cochrane Database Syst Rev, 2, CD002181. Rossing P (2006). Prediction, progression and prevention of diabetic nephropathy. Diabetologia, 49, 11–19. Rule AD (2010). The CKD-EPI equation for estimating GFR from serum creatinine: real improvement or more of the same? Clin J Am Soc Nephrol, 5, 951–3. Stehouwer CDA (2004). Endothelial dysfunction in diabetic neph- ropathy: state of the art and potential significance for non-diabetic kidney disease. Nephrol Dial Transplant, 19, 778–81. Strippoli GFM, et al. (2004). Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists on mortality and renal outcomes in diabetic nephropathy: systematic review. BMJ, 329, 828–40. Study of Heart and Renal Protection website. http://www.sharpinfo. org The Renal Association (2018). UK Renal Registry: 20th annual report of the Renal Association. Nephron, 139 Suppl 1, 1–372. Tuttle KR, et al. (2014). Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes Care, 37, 2864–83. UK Prospective Diabetes Study Group (1998). Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet, 352, 837–53. UK Prospective Diabetes Study Group (1998). Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes (UKPDS 38). BMJ, 317, 703–13. Upadhyay A (2012). Lipid lowering therapy in persons with chronic kidney disease: a systematic review and meta-analysis. Ann Intern Med, 157, 251–62. US Renal Data System (2014). 2014 USRDS annual data report. Volume 1: chronic kidney disease. National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, Bethesda. http://www.usrds.org/adr/htm US Renal Data System (2018). 2018 USRDS annual data report. Volume 2: end stage renal disease (ESRD) in the United States. National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, Bethesda. https://www.usrds.org/adr.aspx White SA, Shaw JA, Sutherland DER (2009). Pancreas transplantation. Lancet, 373, 1808–17. Wolf G, Chen S, Ziyadeh FN (2005). From the periphery of the glom- erular capillary wall towards the centre of disease: podocyte injury comes of age in diabetic nephropathy. Diabetes, 54, 1626–34.

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