Table 21.10.1.2 Natural history of nephropathy in

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section 21 Disorders of the kidney and urinary tract 4980 Prevention Glycaemic control The association of glycaemia and development of nephropathy has led to numerous studies exploring the potential of glycaemic control in the prevention of increases in UAER. The two landmark studies were the Diabetes Control and Complications Trial (DCCT) in type 1 and the UKPDS in type 2 (Table 21.10.1.3). Both compared the intensive management of hyperglycaemia using multiple injections of insulin in type 1, and early use of insulin in type 2, against more conventional control. Those in the intensively treated groups also had more frequent contact with healthcare professionals. The DCCT co- hort was invited to continue surveillance for a further 8 years as part of the Epidemiology of Diabetes Interventions and Complications (EDIC) study. Both DCCT and UKPDS demonstrated a significant reduc- tion in numbers developing moderately increased albuminuria, although there was still a substantial incidence of 15 and 19.2%, respectively, in the intensively treated cohorts (Table 21.10.1.3). Interestingly, the benefit of intensive treatment continued in the EDIC follow-up, despite a deterioration in glycated haemoglobin (HbA1c) to levels close to those seen in the conventional group at 66 mmol/mol (8.2%). Thus a prolonged period of good glycaemic control appears to confer benefit in terms of prevention of compli- cations in the kidney (and the retina) for many years. Moreover, the intensive cohort who were normotensive at the beginning of the EDIC study showed a 32% reduction in the risk of developing hypertension (blood pressure >140/90 mmHg) compared to the conventional group. By contrast, the ACCORD Study of intensive glycaemic control in patients with type 2 diabetes at high cardio- vascular risk failed to demonstrate a benefit in terms of prevention Table 21.10.1.2 Natural history of nephropathy in type 1 diabetesa Normal ↔ Moderately increased albuminuria → Severely increased albuminuria UAER <20 µg/min 1–2% p.a. progress to moderately increased albuminuria 20–200 µg/min (increasing by 20% p.a.) (up to 25% type 1 revert to normal) 1–4% p.a. progress to severely increased albuminuria

200 µg/min GFR Stable: declines at 1 ml/min per year from over 40 years of age Age-related changes until UAER approaches 200 µg/ min or if blood pressure increases Declines at 10 ml/min per year (hypertensive), 4 ml/min per year (normotensive) Blood pressure Stable: significantly higher in those progressing to microalbuminuria Initially stable, but higher than normal controls. Tends to increase with increasing UAER Most patients hypertensive (>140/90 mmHg) Increases with declining GFR Pathology Large kidneys Tubular hypertrophy/ hyperplasia Glomerular enlargement— normal ultrastructure, but glomerular basement membrane thickening 20 nm p.a. Kidneys can remain large Glomerular basement membrane thickening 54 nm p.a. Mesangial expansion 4% p.a. Kidneys tend to shrink Glomerular basement membrane 2–3 times normal thickness, but stable Nodule formation Global glomerulosclerosis Mesangial expansion c.7% p.a. GFR, glomerular filtration rate; p.a., per annum; UAER, urinary albumin excretion rate. a Fewer data in type 2 patients, many of whom are hypertensive at diagnosis. Table 21.10.1.1 Levels of proteinuria, albuminuria, and albumin:creatinine ratio (ACR) that define normal, moderately increased (microalbuminuria), and severely increased albuminuria (clinical proteinuria). Borderline results should be repeated on early morning samples or confirmed by a timed collection 24-h urine Timed overnight ‘Spot’ samplea, b Total protein
(g/day) Albumin
(mg/day) Albumin
(µg/min) Albumin concentration (mg/litre) ACR
(mg/mmol) ACR
(mg/g) Normal <0.15 <30 <20 <20 <2.5 male <3.5 female <20 male <40 female Moderately increased albuminuria (microalbuminuria) 30–300 20–200 50–300 2.5–30 male 3.5–30 female 20–300 male 40–300 femalec Severely increased albuminuria (clinical proteinuria) 0.5 300 200 300 30 300 a False-positive results with diurnal variation, exercise, urine infection, other renal disease, haematuria, or heart failure. b False-negative results with dilution or diuresis. c American Diabetes Association uses a definition of 30–300 mg/g for both males and females.

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