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concentrations ($p < 0.01$). In contrast, the intracellular inositol concentration remained unchanged ($0.156 \pm 0.012 \mu\text{g } 10^6 \text{ cells}^{-1}$ vs $0.133 \pm 0.015 \mu\text{g } 10^6 \text{ cells}^{-1}$). Inositol transport rates and Na^+/K^+ ATPase activity were also unaffected by changes in intracellular sorbitol concentrations: Inositol transport $V_{\max} 5.10 \pm 0.89 \text{ pmol min}^{-1} 10^6 \text{ cells}^{-1}$ vs $5.34 \pm 0.88 \text{ pmol min}^{-1} 10^6 \text{ cells}^{-1}$; $K_m 41.0 \pm 5.2 \mu\text{M}$ vs $48.6 \pm 5.4 \mu\text{M}$; Na^+/K^+ ATPase activity (Rb⁸⁶ assay) 35.2 ± 7.2 vs $34.7 \pm 5.0 \text{ DPM min}^{-1} 10^6 \text{ cells}^{-1}$.

These results clearly demonstrate that changes in the intracellular sorbitol concentration do not exert direct effects on intracellular inositol concentration, inositol transport rates or Na^+/K^+ ATPase activity. These observations have important implications for the polyol theory.

P36. Ascorbic acid depletion in patients with Type 2 diabetes consuming adequate dietary vitamin C.

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Disturbances of vitamin C (ascorbic acid, AA) metabolism in diabetes have been frequently reported, and although free radical mechanisms have been linked to this phenomenon, the exact underlying mechanism is unknown. Since dietary inadequacy of vitamin C may be a potential factor in diabetic patients, we measured vitamin C intake, using a 4 day food diary and vitamin C questionnaire, in a group of 30 age-matched healthy controls (age 68.8 ± 6.9 ; 17 M/13 F) and in a group of 30 age-matched healthy controls (age 68.0 ± 5.5 ; 12 M/18 F). In addition, venous blood samples were taken for measurement of plasma AA, dehydroascorbic acid (DHA), glucose and fructosamine in 20 subjects in each group. Plasma concentrations of AA and DHA were significantly lower in patients than in controls, AA: 29.1 ± 19.2 vs 68.8 ± 36.0 , $p < 0.0001$; DHA: 27.5 ± 6.6 vs 31.8 ± 4.8 , $p < 0.01$. No significant differences in AA intake were seen between the groups using either method: 1. 4 day diary: 61 ± 28 (patients) vs 69 ± 33 (controls) mg day^{-1} ; 2. questionnaire: 54 ± 29 (patients) vs 65 ± 31 (controls). Plasma AA and mean dietary AA intake over 4 days was significantly correlated: $r = 0.49$, $p < 0.01$.

In conclusion, 1. Diabetes is associated with a marked reduction in plasma AA; 2. AA depletion appears to be a direct consequence of the diabetic process rather than due to inadequate dietary AA intake; 3. AA supplementation of the diet in diabetes may be necessary to maintain satisfactory vitamin C status.

P37. A comparison of pancreatic ductal and interstitial collagenase injection in porcine islet isolation.

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The most efficient method of islet isolation in many mammalian species results from injection of collagenase into the pancreatic duct. In this study, the effect of interstitial and intraductal injections of collagenase on the isolation of porcine islets has been assessed.

Pancreata obtained from a slaughterhouse were transected: The duct of one half was cannulated and the gland distended with collagenase (A); collagenase was injected in the other half at multiple sites (B). The islet isolation procedures thereafter were identical. Islets yields were determined by counting dithizone stained cell clusters.

The numbers of islets isolated by each method were not significantly different: 17867 ± 6373 per g pancreas (mean \pm SD) (A) and 21733 ± 8065 per g pancreas (B) ($p > 0.2$; $n = 7$). The number of islet equivalents, assuming a standard islet diameter of $150 \mu\text{m}$, was 2423 ± 795 (A) and 2797 ± 1149 (B). However, 10% of islets isolated using intraductal collagenase were $100\text{--}200 \mu\text{m}$ diameter, whereas only 3% of islets obtained after multiple injection of collagenase were in this size range. Islets from both groups increased insulin secretion in response to glucose stimulation *in vitro*.

In conclusion, injection of collagenase into the pancreatic duct system does not result in greater yields of porcine islets than injection of the enzyme at multiple sites throughout the gland.

P38. Variability of the rate of absorption of soluble insulin and resulting hypoglycaemic effect: influence of injection site.

Vora J., Burch A., Peters J. R., Owens D. R. Department of Medicine, University of Wales College of Medicine, Cardiff.

The variability in the absorption of ^{125}I -soluble insulin and its hypoglycaemic effect over 6 h were compared for the abdominal wall, thigh and upper arm regions in 6 normals (age: 23–27 yr; Body Mass Index: $18.2\text{--}24.1 \text{ kg m}^{-2}$). Each site was assessed on two separate occasions, in a randomized order. Absorption of 6 U ^{125}I -soluble insulin, including during the early lag-phase of slow absorption, was determined using 2 and 3 parameter biexponential models' description of residual radioactivity at injection sites-time curves, and plasma insulin levels. Absorption of soluble insulin was significantly faster with shorter duration lag-phase and earlier maximal hypoglycaemic effect for the abdominal site compared with the thigh and arm ($p < 0.05\text{--}0.001$), with no significant differences between the latter two sites. Within- (CV_w) and between-subject (CV_b) coefficients of variation for insulin absorption rate-constants of 15–29% and 23–38% were similar for the three sites, as were CV_w and CV_b for the lag-phase parameters at 5–20% and 20–40% respectively. CV_w for plasma glucose levels over the 6 h period ranged between 5–20% for the three sites, whilst CV_b increased gradually from 5–10% prior to soluble insulin to 22–28%, coinciding with plasma glucose nadirs. Thus, despite regional differences in the rate of absorption of soluble insulin, within- and between-subject variability in its absorption and hypoglycaemic effect are of similar magnitude for the three sites.

P39. Vanadate lowers blood glucose in diabetic rats by suppressing food intake: absence of a specific anti-diabetic action.

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Vanadate mimics insulin action *in vitro*, lowers blood glucose in diabetic rats, and has been suggested as a novel

treatment for diabetes. However, it also inhibits feeding which itself could lower blood glucose. We assessed the contribution of hypophagia to vanadate's anti-hyperglycaemic action in a 3-week study of streptozotocin-diabetic (STZ-DM) rats. Untreated diabetics ($n=8$) ate significantly more than non-diabetic controls ($n=8$; food intake, 68 ± 3 (SEM) vs 44 ± 1 g rat⁻¹ day⁻¹, $p < 0.001$). Diabetic rats ($n=8$) given sodium metavanadate (0.5 mg in 0.5 ml water by gavage twice-daily after diabetes induction) had significantly lower food intakes (41 ± 2 g rat⁻¹ day⁻¹, $p < 0.001$) than untreated diabetics. Vanadate-treated diabetic rats had significantly lower blood glucose levels (average after 5 days, 16.5 ± 3.0 mmol l⁻¹) than untreated diabetics (38.2 ± 3.4 mmol l⁻¹, $p < 0.001$). However, diabetic rats ($n=8$), not given vanadate but restricted to the food intake of the vanadate-treated diabetics, showed virtually identical blood glucose falls to 17.8 ± 2.6 mmol l⁻¹ ($p < 0.05$ vs vanadate-treated diabetics). In non-diabetic rats ($n=8$), vanadate significantly reduced food intake to 33 ± 1 g rat⁻¹ day⁻¹ ($p < 0.05$ vs untreated non-diabetics) but did not significantly affect blood glucose (7.7 ± 1.1 mmol l⁻¹ vs 9.1 ± 0.6 mmol l⁻¹ in untreated non diabetics; $p > 0.05$).

The glucose-lowering effect of vanadate in STZ-DM rats is therefore due entirely to its suppression of feeding. It may have no specific anti-diabetic action *in vivo*.

P40. Diabetes in the elderly: a population based cohort study on the effect of glucose tolerance on mortality.

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Many consider the effect of diabetes in the elderly is mild: we have examined how mild. We determined the mortality of the Melton Mowbray cohort that we have studied previously. Melton residents aged 65, 70, 75, 80 or 85 yr on 1.8.87 were screened using a 2 h plasma glucose post 75 g oral glucose. If the glucose was more than 11 mmol l⁻¹ the test was repeated. The population was divided into known diabetics ($n=52$), discovered diabetics ($n=18$), impaired glucose tolerance, (IGT, $n=44$), normal glucose tolerance ($n=520$) and refused ($n=191$). Death certification was obtained from the Office of Population Census and Survey and from General Practitioners. After 53 months 11% of normals, 52% of known diabetics, 39% of discovered diabetics, 20% of those with IGT and 18% of refusals had died. Using Cox's proportional hazards regression model, with age and sex as strata, the relative risk (RR) of death (95% confidence intervals), compared with normals was 4.5 (2.9-7.0) in all diabetics, 5.2 (3.2-8.5) in known diabetics, 3.0 (1.3-6.6) in discovered diabetics, 1.7 (0.8-3.5) in IGT and 1.5 (1.0-2.4) in refusals. The known diabetics had a significantly higher mortality than discovered diabetics. (RR 1.8 (1.2-2.6)). In the elderly known diabetes and diabetes discovered by screening considerably increase mortality.

P41. A District Diabetes Register is feasible: more patients than expected.

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Audit is a tool for ensuring the comprehensiveness and quality of health care delivery. The impact of diabetes and

its complications can be reduced by well organized, integrated care and many important outcome measures are well recognized. But diabetes health care audit is a daunting task because the patient population is very large and widely dispersed between and within different levels of care. Thus, establishing a population based District Diabetes Register seems an inescapable prerequisite for successful audit. Salford district has a resident population of 228 205 (very few from ethnic minorities). All of the 125 GPs (66 practices) and the three Consultants (two physicians, one paediatrician) with an interest in diabetes are participating in a District Diabetes Audit project. The demographic details of all known diabetic patients have now been registered: 4950 patients (M 49%, F 51%) have been identified representing 2.2% of the population, a higher proportion than anticipated; the interpractice variation in proportion of patients with identified diabetes was appreciable, 1-2.5%; more than half were 40-69 years old—<19 (5.6%), 20-39 (9.6%), 40-59 (28%), 60-69 (24.6%), 70+ (32.2%); 54.2% (29-88) attend hospital, 45.8% (18-71) wholly managed in primary care. In conclusion, establishing a District Diabetes Register is feasible; there is a high prevalence of diabetes in this urban district.

P42. Spatial clustering in childhood onset diabetes during epidemic years: further evidence of an environmental cause.

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We have previously presented evidence in favour of an environmental cause for Type 1 diabetes: it includes a major increase in the incidence of the disease with time; a changing incidence rate on migration; and epidemic peaks of incidence. We have now examined a case-control study comparing primary schools attended in an epidemic year (1986), compared with a non-epidemic year (1990). Our hypothesis: if environmental factors are important, primary schooling would be more likely to be shared by cases in an epidemic year compared with controls. Cases were identified from an established register with known accurate ascertainment; matched controls from age-sex-race-date of birth matched central register of all children (nearest 4); parents were asked to fill out a structured questionnaire on schooling. In 1986, 9 out of 29 cases clustered in primary schooling; 2 of 25 matched controls (4 non-responders), second matched controls 0 of 25 (4 non-responders). This was significantly different (95% confidence limit 0.03 to 0.43, $p < 0.05$). There was no significant difference in the non-epidemic year.

Temporo-spatial clustering occurs in Type 1 diabetes. The environmental factor should be sought during epidemic years, possibly related to schooling, though the vector is unknown.

P43. Smoking is associated with reduced total plasma antioxidant activity in diabetes.

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Free radical attack may damage macromolecules and contribute to the complications of diabetes. Smoking is a risk factor for the development of diabetic complications