Poges, Slough, England). Three days before admission he experienced abdominal pain and nausea after dining out. He maintained his preprandial capillary blood glucose below 10 mmol/L with his usual insulin schedule and a light equivalent diet. Twenty-four hours before admission he began vomiting but was still able to take equivalent amounts of oral glucose. On the morning of admission, capillary blood glucose was 9.0 mmol/L, the patient having taken his normal basal insulin infusion rate (0.6 U/h) for the previous 12 h. He was now feeling thirsty and telephoned the ward for advice. He wanted to continue managing the condition at home; however, his speech sounded "thick" on the telephone and he was advised to come to the ward. On admission 3 h later, he was profoundly dehydrated and ketotic; plasma glucose was 21.7 mmol/L, serum bicarbonate 7.9 mmol/L, serum urea 11.8 mmol/L, and arterial pH 7.1. He was managed with intravenous fluids and additional hourly doses of insulin, and recovered uneventfully.

Case 2: A 24-yr-old female arts graduate with IDDM for 11 yr, on twice-daily subcutaneous insulin, had been self-monitoring with a reflectance meter (Glucometer, Ames) for 2 yr. Two weeks before admission she had a mild abdominal upset with vomiting lasting 4 days, which she managed successfully at home, taking glucose drinks and extra short-acting insulin. Only one capillary blood glucose reading during that time exceeded 10 mmol/L. Four days before the present admission, the patient had further abdominal discomfort with intermittent diarrhea and vomiting. She maintained relatively normal blood glucose readings (only one reading greater than 10 mmol/L) until the morning of admission. By then the reflectance meter read "high" and she was feeling thirsty. After taking an increased morning insulin dose she came to the hospital emergency department. On admission, she was dehydrated and ketotic; plasma glucose was 36.4 mmol/L, serum bicarbonate 11.3 mmol/L, serum urea 13.8 mmol/L, and arterial pH 7.23. After intravenous fluids and hourly supplementary insulin she made a full recovery.

Both of the patients described were intelligent; they tested blood glucose at least four times daily and were regular clinic attenders. It might be expected that such patients would be well equipped to manage intercurrent illness themselves and to avoid hospital admission. Our two patients, while able to manage the early part of their illness adequately, ultimately delayed seeking formal advice until dangerous acidosis had developed.

Patients who are self-monitoring must not forget that severe acidosis may co-exist with normal blood glucose concentrations.[3] Clouding of consciousness may not be prominent in ketoacidosis without hyperglycemia and such patients may appear surprisingly well. Neither of our patients had tested urine for ketones, which might have given early warning of a situation beyond their control. A new generation of patients (and doctors) instructed in the disadvantages of testing urinary rather than blood glucose concentrations needs to be reminded of the value of testing urine for ketones. The development of a reagent strip suitable for quantitative estimation of blood ketone concentrations would be useful for patients attempting to monitor intercurrent illness at home.

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Urinary Cortisol-Creatinine Ratio and Nocturnal Hypoglycemia

Recent reports suggest varying views on the relationship between hypoglycemia and the urinary cortisol-creatinine ratio (UCCR) and the latter's usefulness in monitoring nocturnal hypoglycemia (NH) in insulin-treated diabetic individuals (ITD). Asplin et al.[1] and Seaworth et al.[2] report findings that suggest that the UCCR might be useful in detecting NH, but Scott and Scandrett[3] and Darlow et al.[4] found no clear relationship between episodes of NH and elevated UCCR.

We report the results of a study to find the frequency of NH in a small group of stable and unstable ITD. Seven unstable (either newly diagnosed or known diabetic subjects with poor control) and 20 apparently stable (asymptomatic and normal urine test records and normal and near-normal spot blood glucose levels) diabetic subjects were studied. The patients' characteristics are summarized in Table 1.

Urine was collected as an early morning sample on four consecutive days. Capillary blood on filter paper was obtained from the same subjects at 3 a.m. Details of UCCR and capillary blood glucose determination are described elsewhere.[5]

The mean ± SEM UCCR of the stable and unstable ITD were 11.27 ± 0.90 and 16.71 ± 2.81, respectively (normal controls 8.5 ± 0.40). The normal range of UCCR for our laboratory is considerably lower than other reported values.[2–4,6] The difference is most likely to be attributable to methodology employed in the determination of urinary free cortisol.

Interpreting values of UCCR greater than the normal mean +2 SD as indication of NH, five of the seven unstable diabetic patients had at least one episode of NH in 4 days and 8 of the 20 stable ITD had NH by the same criterion.

TABLE 1
Characteristics of study patients

Parameter	Unstable diabetic patients	Stable diabetic patients
Sex ratio (M:F)	2:5	8:12
Age (yr) (range)	34 ± 4.5 (13–60)	48.2 ± 3.3 (23–78)
Duration of diabetes (mo)	120 ± 3.7 (0.5–250)	130 ± 5.8 (6–386)
Insulin dose (U/kg/24 h)	0.76 ± 0.08 (0.52–1.1)	0.68 ± 0.06 (0.30–1.4)
Single:split injections	0:7	3:17

Values are given as mean ± SEM (range).

On the other hand, taking a papillary blood glucose level of 2.5 mmol/L as hypoglycemic or potentially so, 5 of the 7 unstable and 7 of the 20 stable diabetic patients had at least one episode of NH in 4 nights.

The mean age (51 versus 43 yr) and insulin dosage (0.75 versus 0.65 U/kg/24 h) were higher, though not significantly so at $P < 0.05$, in subjects with elevated UCCR than in subjects with normal UCCR. The mean ± SE 3 a.m. capillary blood glucose level was significantly lower in subjects with raised UCCR (3.32 ± 0.37 mmol/L) than in diabetic subjects with normal UCCR (5.46 ± 0.66 mmol/L), $P < 0.01$. The sex ratio and duration of diabetes were not significantly different between the two groups on the basis of UCCR.

Although no significant relationship was found between insulin dosage and UCCR, there was a tendency toward higher UCCR as insulin dosages increased. Five of fourteen subjects on <0.70 U/kg/24 h of insulin had elevated UCCR while 9 of the 13 subjects on insulin doses of ≥0.70 U/kg/24 h had raised UCCR, $P < 0.01$. Using capillary blood glucose levels, a similar number of subjects were hypoglycemic: 4 of 14 and 6 of 13 subjects, respectively, in the <0.70 U/kg/24 h and ≥0.70 U/kg/24 h insulin subgroups. NH is apparently common in ITD especially in the unstable diabetic patients.[7,8] The high frequency rate of hypoglycemia found in this study is similar to the findings of others.[8,9]

It is significant that the frequency rates of hypoglycemia were similar employing the UCCR and 3 a.m. capillary blood glucose levels. This would appear to support the potential usefulness of the UCCR in the detection of NH. We have also shown that there is a moderate and significant correlation between the UCCR and the blood glucose at 3 a.m. of ITD.[5]

It should be emphasized that NH was not found to occur every night, by either the UCCR technique or the monitoring of 3 a.m. blood glucose, a finding very akin to what Somogyi[10] found many years ago. It is important, therefore, that multiple determinations of UCCR be made in order to detect NH. Application of a generalized normal range of values of the UCCR to a particular patient may be misleading. Subjects with a long history of diabetes may have blunted cortisol response to hypoglycemia and the UCCR values may appear within normal limits after an episode of hypoglycemia.[11] We have observed marked falls in the apparently normal UCCR of some patients after reduction of insulin dosages. The recognition of the dilutional effect pointed out by Seaworth et al.[2] is also very important in the interpretation of the UCCR in the detection of hypoglycemia.

With the current abundance of self blood glucose monitoring devices it should be easy to detect NH, but NH often occurs between 2 a.m. and 4 a.m., a rather inconvenient time to do self blood glucose monitoring. In such situations, the determination of the UCCR from an early morning urine sample might be helpful. The controversies surrounding the usefulness of the UCCR notwithstanding,[1–4] it appears that the UCCR has a role to play in the convenient and simple detection of NH, bearing in mind the various limitations.

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