affinity columns in biochemical experiments and be used to isolate insulin receptors. On the other hand, circulating complexed insulin is always assumed to be biologically active. Vaughan et al.[1] suggest that the antibody might serve as a reservoir for the liberation of free insulin and be beneficial, although Bolli et al.[2] note that the delay in recovery from hypoglycemia might also be due to free insulin released from insulin-antibody binding. It may be that the patient we reported was unique and had widely disparate circulating binding activities that contributed to the hyperglycemia and hypoglycemia. It may also be that insulin bound to her low-affinity antibody maintained biologic activity. We were not successful in our first attempt at developing an in vitro assay for evaluating the biologic activity of the bound insulin. We were able to measure biologic activity in the patient herself.

STEWART G. ALBERT, M.D.
DENNIS A. POPP, M.D.

From the Division of Endocrinology, Department of Internal Medicine, St. Louis University School of Medicine, 1402 S. Grand Blvd., St. Louis, Missouri 63104.

REFERENCES

[1] Vaughan, N. J. A., Matthews, J. A., Kurtz, A. B., and Nabarro, J. D. N.: The bioavailability of circulating antibody-bound insulin following insulin withdrawal in type I (insulin-dependent) diabetes. Diabetologia 1983; 24:355–58.

[2] Bolli, G. B., Dimitriadis, G. D., Pehling, G. B., Baker, B. A., Haymond, M. W., Cryer, P. E., and Gerick, J. E.: Abnormal glucose counterregulation after subcutaneous insulin in insulin dependent diabetes mellitus. N. Engl. J. Med. 1984; 310:1706–11.

Insulin Wastage

On reading the article entitled "Insulin Wastage in Ambulant Practice," which appeared in the July-August issue of DIABETES CARE,[1] I was struck with amazement and incredulity. The authors compared the amount of insulin purchased by insulin-dependent diabetic patients over the course of 2 yr with the amount they should have used based on their recommended dosage. They found an excess of the amount purchased over the amount prescribed, which they termed "wastage." The authors discuss a variety of reasons for this "wastage" focusing entirely on the type of syringe used, and the technique of insulin withdrawal from the vial.

The amazement and incredulity derive from the apparent belief of the authors that the subjects never deliberately deviated from the prescribed amount of insulin. As both an insulin-dependent diabetic person and a psychologist, it seems obvious to me that most people could not possibly follow exactly, over the course of 2 yr, the rigid regimen prescribed for diabetic individuals. This is certainly true with regard to diet.[2] Deviations in the direction of undereating are not significant since the penalty (insulin reaction) forces a remediation. But deviations in the direction of overeating are often compensated for by the administration of extra insulin. Thus, I would urge the authors to consider that the "wastage" they discovered may in part be due to their subjects "covering" additional food. I call this the "chocolate cake factor."

I also caution that acknowledgment of this behavior might be difficult to obtain without guarantees of anonymity. The medical profession reacts with such disapprobation to such admissions on the part of patients, that patients are loath to disillusion the professionals.

After years of being a diabetic patient and encountering a variety of diabetologists, I continue to be amazed at the idealism of these professionals. An assumption seems to be made that patients will do whatever is prescribed, regardless of its rigor or interminability. The reality is that diabetic patients are also people with habits and needs who are vulnerable to many more influences and pressures than this one aspect of their lives, however important this condition may be. Isn't it time that professionals recognize this truth and deal with their patients/subjects in a realistic rather than an idealistic manner?

ESTHER DAMASER, Ph.D.

Address reprint requests to Esther Damaser, Ph.D., 830 Xenia Avenue, Yellow Springs, Ohio 45387.

REFERENCES

[1] Berne, C., Agenas, I., Eriksson, G., and Wibell, L.: Insulin wastage in ambulant practice. Diabetes Care 1984; 7:343–46.

[2] Wing, R. R., Epstein, L. H., and Nowalk, M. P.: Dietary adherence in patients with diabetes. Behav. Med. Update 1984; 6:17–21.

Insulin Wastage: A Reply

We fully agree with Dr. Damaser's statement that a realistic attitude rather than an idealistic one is the best basis for our role as advisors to diabetic patients. During diabetic summer camps we have had the opportunity to share the daily life of young adult diabetic patients, which has helped us to gain some insight into what insulin-dependent diabetic patients can do and can be motivated to do. Adjustments of life-style to a diabetic regimen are particularly complicated for many young people. One minor aspect of this is the difficulty to abstain from extra carbohydrate, the so called "chocolate cake factor."

However, the calculations from our study (DIABETES CARE 1984; 7:343–46), based on a practical test of insulin withdrawal carried out by 101 patients, show that technical factors rather than taking extra insulin account for most of the discrepancy between purchased and injected insulin, i.e., the "insulin wastage." The *daily* wastage was found to be 16.9 U of insulin (U40). Using a syringe with a separate needle (large dead space) and adjusting the insulin dose by injecting surplus insulin into the air leads to a daily measured loss of 11.6 U of U40 insulin for patients on a two-dose regimen. The figure

of course increases 250% if U100 insulin is used. Using syringes with fixed needles (small dead space) and injecting the insulin surplus back into the bottle, a daily loss of 1–2 U will occur.

In addition, we have now carried out an anonymous inquiry in a group of 53 insulin-dependent patients. When asked about how often they changed their insulin doses and the magnitude of the dose change, 70% admitted deviations from the habitual dose (a term that we prefer to "recommended," since we encourage rather than discourage our patients to adjust insulin doses before extra meals, sports activities, or according to the results of self-monitoring of blood glucose). Eight percent of the patients changed doses daily and 50% one day weekly or monthly. The daily dosage adjustments averaged 3.4 U. Furthermore, there was a slight predominance of those who lowered the dose over those who took extra insulin.

The results of the inquiry thus demonstrate that extra insulin could have had no or only a minor influence on our calculated wastage of insulin. Neither is it reasonable to assume that a significant upward trend in the insulin doses could have infuenced the results, since the "recommended" doses were reevaluated every third month during the 2-yr period of investigation.

CHRISTIAN BERNE, M.D.
INGEGERD AGENÄS, Pharm.D.
GUNNAR ERIKSSON, Pharm.D.
LARS WIBELL, M.D.

From the Department of Internal Medicine, University Hospital, Uppsala, Sweden (C.B., L.W.); the National Corporation of Swedish Pharmacies, Stockholm, Sweden (I.A.); and Kronan Pharmacy, Uppsala, Sweden (G.E.).

Which Patients Might Benefit from Combining a Sulfonylurea with Insulin?

Combining a sulfonylurea with insulin is an obvious but little-tested therapeutic option for type II diabetes. While published experience is scanty,[1–5] we believe empirical use of combination therapy is common. Available data suggest that responses to this approach are highly variable between individual patients. Therefore, information regarding which patients are the best candidates is needed.

A number of our patients, in efforts to improve on prior suboptimal glycemic control, have used a regimen combining bedtime intermediate-acting insulin with daytime sulfonylurea (BIDS). This approach is designed to control fasting glycemia, including the "dawn phenomenon," with bedtime insulin, while enhancing daytime glycemic control with tolazamide. We have reviewed the outcome for 22 patients (5 men, 17 women; age 53–73 yr; relative body weight by 1983 Metropolitan Life tables 100–180%; duration of diabetes 1–25 yr) with enough follow-up data, including a 4-mo period on prior therapy and between 4 and 8 mo on BIDS. Prior therapies included tolazamide (500–1000 mg/day, N = 4), a single insulin injection (14–48 U/day, N = 5), and multiple injections (22–100 U/day, N = 13). On BIDS, patients took 250–500 mg tolazamide in one (acB) or two (acB, acL) doses, and lente or NPH insulin at bedtime, the doses at last follow-up ranging from 12 to 90 U/day, mean ± SD 32 ± 21 U/day. Insulin doses were adjusted according to clinical judgment and, for the patients previously using insulin, averaged 79% of the original dose at last follow-up. Glycosylated hemoglobin (GHb, colorimetric, normal mean ± SD = 7.0 ± 1.5 $\%A_1$) was unchanged from baseline (10.7 ± 0.4 $\%A_1$, mean N of samples = 2.7/patient) to follow-up (10.4 ± 1.1 $\%A_1$, mean N of samples = 2.7/patient). However, the change of GHb (ΔGHb) from baseline to follow-up showed, by multiple correlation analysis, significant correlations with relative body weight ($P < 0.01$) and duration of diabetes ($P < 0.05$), a decline of GHb on BIDS being associated with leanness and short duration. These relationships are shown another way in Figure 1. A significant correlation between relative body weight and GHb was apparent ($r = 0.424$, $P < 0.05$). When patients with diabetes >12 yr (open circles) were excluded, a stronger correlation (N = 13, $r = 0.819$, $P < 0.001$) was evident.

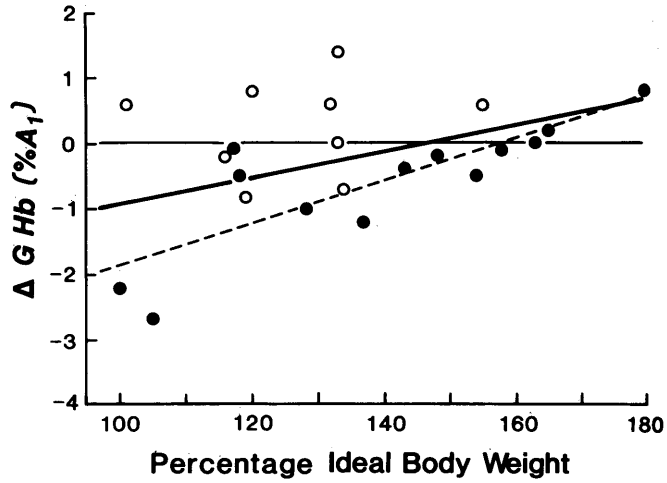

FIG. 1. The relationship between glycemic outcome on BIDS (ΔGHb) and relative body weight for 22 patients with type II diabetes. Improved mean plasma glucose is suggested by a negative ΔGHb. Closed circles represent 13 patients with diabetes ≤12 yr; open circles represent 9 patients with diabetes of longer duration. The solid line represents the linear regression for all patients ($y = -2.76 \pm 0.019x$, $r = 0.424$, $P < 0.05$); the interrupted line represents that for the patients with diabetes ≤12 yr ($y = -5.07 \pm 0.032x$, $r = 0.819$, $P < 0.001$). In each case there is a significant relationship between leanness and favorable glycemic outcome on BIDS.

These preliminary findings suggest relatively nonobese persons with short duration of type II diabetes are the best can-