Impact of Fat, Protein, and Glycemic Index on Postprandial Glucose Control in Type 1 Diabetes: Implications for Intensive Diabetes Management in the Continuous Glucose Monitoring Era

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BACKGROUND

Continuous glucose monitoring highlights the complexity of postprandial glucose patterns present in type 1 diabetes and points to the limitations of current approaches to mealtime insulin dosing based primarily on carbohydrate counting.

METHODS

A systematic review of all relevant biomedical databases, including MEDLINE, Embase, CINAHL, and the Cochrane Central Register of Controlled Trials, was conducted to identify research on the effects of dietary fat, protein, and glycemic index (GI) on acute postprandial glucose control in type 1 diabetes and prandial insulin dosing strategies for these dietary factors.

RESULTS

All studies examining the effect of fat ($n = 7$), protein ($n = 7$), and GI ($n = 7$) indicated that these dietary factors modify postprandial glycemia. Late postprandial hyperglycemia was the predominant effect of dietary fat; however, in some studies, glucose concentrations were reduced in the first 2–3 h, possibly due to delayed gastric emptying. Ten studies examining insulin bolus dose and delivery patterns required for high-fat and/or high-protein meals were identified. Because of methodological differences and limitations in experimental design, study findings were inconsistent regarding optimal bolus delivery pattern; however, the studies indicated that high-fat/protein meals require more insulin than lower-fat/protein meals with identical carbohydrate content.

CONCLUSIONS

These studies have important implications for clinical practice and patient education and point to the need for research focused on the development of new insulin dosing algorithms based on meal composition rather than on carbohydrate content alone.

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Currently, carbohydrates are considered the predominant macronutrient affecting postprandial glucose control and the primary determinant for calculating mealtime insulin doses in type 1 diabetes (1). Emerging evidence from recent research and the use of continuous glucose monitoring have shown that other nutritional properties of food, including fat, protein, and glycemic index (GI), can significantly affect postprandial glucose excursions. These findings highlight the need for alternative mealtime insulin dosing algorithms and have important implications for nutrition education and counseling in patients with diabetes.

The American Diabetes Association (ADA) recommends that people with diabetes who have mastered carbohydrate counting receive education on the glycemic impacts of protein and fat (1). To our knowledge, neither a comprehensive review of the literature examining the relative effects of protein, fat, and GI on postprandial glycemia nor guidelines for clinicians on how insulin doses should be adjusted in type 1 diabetes for various meal compositions exist.

This article reviews the evidence addressing the following questions:

1. What effects do GI, protein, and fat have on acute postprandial glucose concentrations in type 1 diabetes?
2. What prandial insulin dosing strategies work best for GI, protein, and fat in type 1 diabetes?

In light of the evidence reviewed in these questions and our clinical insights, this article also discusses the following questions:

3. What are the implications for clinical practice?
4. What are the knowledge gaps, and how can technology be leveraged to improve postprandial glucose control?

Current clinical approaches to intensive diabetes management tend to be insulin-centric; however, a focus on dietary quality and mealtime routine, with referral to a registered dietitian for medical nutrition therapy, may be just as important for optimizing glycemic control (1,2). In the coming years, as continuous glucose monitoring becomes the standard of care in the management of type 1 diabetes (3), the challenges of keeping postprandial glucose concentrations in range will become an inescapable and increasing focus in the daily lives of people with diabetes.

SYSTEMATIC REVIEW PROCEDURE

For questions 1 and 2, a search of all relevant biomedical databases was conducted, including MEDLINE, Embase, CINAHL (Cumulative Index to Nursing and Allied Health Literature), Thomson Reuters Web of Science (formerly ISI Web of Knowledge), and the Cochrane Central Register of Controlled Trials. The following key words were used to identify potentially relevant articles: "type 1 diabetes" AND "blood glucose" OR "insulin" AND "dietary carbohydrate" OR "dietary protein" OR "dietary fat" OR "glycemic index." The search strategy was deliberately broad to identify all relevant articles to answer the two review questions.

Original controlled studies were included if they were published in English between March 1995 and November 2014, conducted in adults and/or children with type 1 diabetes, used rapid-acting insulin analogs (lispro, aspart, or glulisine), and *1*) compared postprandial glycemia following different foods/meals with the same insulin dosing strategy or *2*) different prandial dosing strategies for the same foods/meals. A start date of March 1995 was intentionally chosen because this was when the first rapid-acting insulin analog (lispro) was available in the U.S. Studies of participants of any age, sex, or race were included. Studies where both the meal and the insulin dose were concurrently altered or the meal composition was not controlled and studies in pregnancy or involving exercise were excluded.

The literature search identified 143 studies, and 13 more studies were identified through hand-searching reference lists (Supplementary Fig. 1). Of these studies, 127 were excluded primarily due to duplication (n = 23) and not meeting the inclusion criteria for this review, including 21 in type 2 diabetes, 6 comparing various types of insulin or regimens, and 4 varying insulin dosing and meals concurrently. The remaining 29 studies were included in this review.

QUESTION 1: WHAT EFFECTS DO GI, PROTEIN, AND FAT HAVE ON ACUTE POSTPRANDIAL GLUCOSE CONCENTRATIONS IN TYPE 1 DIABETES?

As summarized in Table 1, 16 studies examining the effects of nutritional factors on postprandial glycemia were identified (4–19) (see Supplementary Table 1 for more details).

Fat

Seven studies examining the effect of dietary fat on postprandial glycemia in 103 subjects with type 1 diabetes were identified (5,7,8,11,15,18,19). All studies added fat to the test meal, which concurrently increased the energy content of the test meal. The amount of dietary fat added to the control meals ranged from 6.6 to 52 g.

All studies reported that dietary fat modified postprandial glycemia. One study did not find an increase in glucose concentration (5) possibly because the postprandial monitoring period was only 3 h. Two studies reported that the addition of dietary fat reduced the area under the curve in the first 2–3 h (7,8). This may be due to fat delaying gastric emptying, as indicated by one of the studies demonstrating that the gastric emptying rate was significantly reduced in the first 2 h after consuming a high-fat meal (7). This in turn delayed the rise in postprandial glycemia, with four studies reporting a lag in time to peak blood glucose concentrations between 6 and 90 min (mean 29 min) (5,7,15,18).

Evidence suggests that meals containing carbohydrates and that are high in dietary fat cause sustained late postprandial hyperglycemia. One study showed the addition of 35 g dietary fat significantly increased postprandial glucose concentrations by 2.3 mmol/L at 5 h (15). Wolpert et al. (19) demonstrated that the addition of 50 g fat caused significant hyperglycemia over 5 h, even when additional insulin was administered using a closed-loop glucose control system. Free fatty acids (FFAs) directly induce insulin resistance, and one study postulated that the mechanism for the delayed hyperglycemic effect of dietary fat is FFA-induced insulin resistance with increased hepatic glucose output (20). Consistent with the observed time course of hyperglycemia following higher-fat meals in type 1

Table 1—Summary of systematic review: effects of fat, protein, and GI on acute postprandial glycemia in type 1 diabetes

Nutritional factor	Summary of findings	Clinical implications
Fat	• Seven studies (total 103 subjects) (5,7,8,11,15,18,19). • All studies reported significant differences in glycemia with addition of fat. • Fat reduces early glucose response (first 2–3 h) (7,8) and delays peak blood glucose (5,7,15,18) due to delayed gastric emptying. • Fat leads to late postprandial (>3 h) hyperglycemia (18,19). • Addition of 35 g fat can increase blood glucose by 2.3 mmol/L (15), and in some individuals, 50 g of fat can increase insulin requirements by twofold (19). • Marked interindividual differences in the glycemic effect of fat.	• Increase in dose required for coverage of higher-fat meals needs to be individualized. • Delicate balance in calculation and timing of insulin action: needs more insulin to prevent late postprandial hyperglycemia; however, if too much insulin upfront, there is a risk for early postprandial hypoglycemia.
Protein	• Seven studies (total 125 subjects) (5,8,11,13,15–17). • All studies reported significant differences in glycemia with addition of protein. • Effect of protein is delayed (effects seen ~100 min postmeal) (11,13,15,17). • Protein has different effects when consumed with and without carbohydrates [e.g., 30 g protein with carbohydrates will affect blood glucose (15,16), whereas at least 75 g protein is needed to see an effect when consumed in isolation (13)].	• Protein-only meals (e.g., ≥230 g lean steak with salad) may require a different insulin dosing strategy than for protein and carbohydrate meals.
GI	• Seven studies (total 98 subjects) (4,6,8–10,12,14). • All studies reported significant differences in glycemia with differing GI (same carbohydrate). • High-GI foods have rapid glucose spike (9,14). • Low-GI foods lower overall glucose response (8–10,12,14), reduce glucose peak (4,9,14), and increase risk of hypoglycemia (when usual CIR is used) (6,9,10).	• Mismatch between insulin action and carbohydrate absorption following high-GI foods can be problematic, leading to a rapid glucose spike. • Total carbohydrate content still important: a large carbohydrate serving of low-GI food will still cause large glycemic response. • Low-GI foods with high fructose and/or sucrose content (e.g., fruit juice) will still produce a rapid glucose spike.

See Supplementary Table 1 for details.

diabetes, Gormsen et al. (21) demonstrated in healthy subjects that insulin resistance develops at least 120 min after circulating FFAs increase.

Protein

Seven studies examining the effect of dietary protein on postprandial glycemia in 125 subjects with type 1 diabetes (range 8–33 subjects) were identified (5,8,11,13,15–17). All studies kept carbohydrate content consistent, with six adding protein to the test meal, thereby concurrently increasing the energy content. Winiger et al. (17) was the only study to keep energy levels constant; however, to keep energy and carbohydrates constant, both protein and fat were simultaneously varied.

All included studies reported that postprandial glycemia was modified by the addition of protein, with all but one (5) reporting significant differences. Smart et al. (15) reported that the addition of 35 g protein to 30 g carbohydrates significantly increased blood glucose levels by 2.6 mmol/L at 5 h. The effect of fat and protein was additive, with blood glucose concentrations increasing by 5.4 mmol/L at 5 h, the sum of the individual incremental increases for protein and fat. Paterson et al. (13) was the only study examining the effect of protein only (in the absence of carbohydrates and fat) and found that the addition of 12.5–50 g protein did not significantly affect glycemia, although the addition of 75 and 100 g significantly increased glucose concentrations, reaching a peak at the conclusion of the 5-h study and causing an increase in glucose concentrations similar to that of 20 g carbohydrates given without insulin. These results suggest that protein has differential effects when consumed with and without carbohydrates.

All studies agreed that protein affects blood glucose concentrations in the late postprandial period. When protein was the only macronutrient consumed, glucose concentrations began to rise after 100 min for protein loads of ≥75 g (13). For meals where carbohydrates were also consumed, increased glucose concentrations were noted after 3–4 h (11,15,17).

Glycemic Index

Seven studies examining the effects of GI on postprandial glycemia in 98 subjects with type 1 diabetes (range 8–20 subjects) were identified (4,6,8–10,12,14). All studies compared higher- versus lower-GI foods or meals. Two studies concurrently varied the energy and macronutrient compositions of the test meals, confounding the interpretation (4,8).

All seven studies reported significant differences in blood glucose concentrations, with low-GI foods and meals producing lower glycemic responses. Three studies suggested that the risk of mild hypoglycemia is greater with low-GI than with high-GI foods (6,9,10); however, the timing of the episodes was not reported. One study suggested that low-GI foods are more likely to cause early hypoglycemia, reporting a correlation between GI and time to hypoglycemia, with each unit increase in GI

delaying hypoglycemia by 1 min (9). This is consistent with the reduced overall glycemic response with low-GI foods/meals.

QUESTION 2: WHAT PRANDIAL INSULIN DOSING STRATEGIES WORK BEST FOR GI, PROTEIN, AND FAT IN TYPE 1 DIABETES?

Fifteen studies examining the effects of varying prandial dosing strategies, including various bolus types, timing of the meal bolus, and methods to calculate the bolus dose, on postprandial glycemia were identified (14,19,22–34) (Supplementary Table 2).

Fat and Protein

Ten studies examining insulin bolus dose and delivery patterns and timing required to cover meals high in fat and/or protein were identified (19,22–24,26–30,33).

Insulin Dose

As summarized in Table 2, six studies investigated the additional insulin requirements for food or meals high in fat or protein (19,22,23,28,29,33). The amount of additional insulin varied across studies depending on the method used to estimate the bolus insulin requirements. Lee et al. (29) used a predetermined value of 50% of the carbohydrate-to-insulin ratio (CIR) to calculate fat-to-insulin and protein-to-insulin ratios, with the additional insulin delivered as an extended bolus. Similarly, another two studies (28,33) calculated additional insulin for fat-protein units (FPUs) (defined as 100 kcal or 420 kJ fat and/or protein) (35), with the duration of the extended bolus adjusted from 3 to 6 h depending on the number of FPUs consumed. A major limitation of this equation was the high rate of clinically significant hypoglycemia compared with carbohydrate counting (28,33). Another study using closed-loop glucose control measured the additional insulin required to maintain glucose control after a high-fat meal (19). This study revealed that the addition of 50 g of fat markedly increased insulin requirements over the 5-h postprandial period, with one subject needing a more than twofold increase. This study identified marked interindividual differences in fat sensitivity, highlighting the need for individualized incremental dosing for fat and pointing to the limitations of equations that calculate individual insulin dosing for fat and protein as a proportion of the individual's CIR (28,29,33).

Two studies investigated another novel insulin dosing algorithm, the Food Insulin Index (FII), to calculate the insulin demand for individual foods (23) and mixed meals (22). The FII is based on the physiological insulin demand evoked by 1,000-kJ food portions as measured in healthy subjects. Because food energy is the constant, the method accounts for all nutritional and metabolic factors that influence insulin demand, not just the macronutrient content. With this method, bolus insulin is calculated for foods not traditionally covered by insulin, including eggs and steak. Both studies reported significantly improved glycemia in the 3-h postprandial period. However, the relatively short postprandial monitoring period may not have detected the delayed glycemic impact of fat and protein. The rates of hypoglycemia were high in both the FII and the carbohydrate-counting groups in one study (23), suggesting that the initial CIR and basal rates were not adequately optimized at study commencement. A pilot study using the FII in practice did not find an increased risk of hypoglycemic events (36).

Table 2—Summary of systematic review: studies evaluating prandial insulin dosing equations and requirements for high-fat meals with or without protein

Method[a]	Limitation
Two studies (28,33) calculated additional insulin for fat and protein using a complex dosing equation with FPUs (35) and the subject's CIR.	High rate of clinically significant postprandial hypoglycemia compared with carbohydrate counting.
One study (29) used a predetermined value of 50% of the CIR to calculate fat-to-insulin and protein-to-insulin ratios and added the additional insulin to extended bolus.	Suboptimal postprandial glucose control.
Two studies (22,23) used the FII to calculate additional insulin for high-fat and/or -protein meals. Both studies reported significantly improved glycemia in the 3-h postprandial period.	Because of the short postprandial monitoring period, may have failed to detect delayed impact of fat and protein on glucose concentrations.
One study (19) used closed-loop control to determine additional insulin required to maintain postprandial glycemic control after a high-fat meal; definitively established that high-fat meals need more insulin coverage than lower-fat meals with identical carbohydrate content.	Findings need to be translated into a dosing equation for use in clinical practice.

See Supplementary Table 2 for details. [a]Method used to calculate the additional insulin and the amount given varied across studies.

Bolus Timing and Type

Whereas all the studies in the literature examining the optimal timing of the prandial bolus (25,26,34) uniformly demonstrated that delivering a bolus 15–20 min before eating rather than immediately before or after the meal significantly improves postprandial glycemia, studies examining the optimal bolus type required to cover higher-fat meals showed discrepant results. Four studies reported that the combo wave bolus was the most effective method (24,27,29,33), whereas one suggested that the standard bolus with insulin delivered 15 min before the meal was superior (26) and another reported no differences in glucose excursions among normal, combo wave, and extended boluses after pasta meals (30).

Methodological differences and issues confound the evaluation of the published literature. The duration and split of the bolus types varied across studies. Furthermore, failure to optimize basal rates as part of the study protocol could have affected the findings of some studies. In addition, differences in the GI and macronutrient content of the test meals and duration and split of the bolus types in the studies may have contributed to the differences in the results. Of note, some studies had a relatively short postprandial monitoring period

and, thus, may not have detected the delayed hyperglycemia from dietary fat.

Glycemic Index

Two studies examining insulin dosing strategies to improve postprandial glycemia for low-GI meals were identified (14,32). One study in patients using a pump demonstrated that a 50:50% combo wave bolus over 2 h resulted in a 47% decrease in the postprandial glucose area under the curve compared with a standard bolus for a low-GI meal (32). Another study examined bolus strategies for low-GI meals in children using multiple daily injections and found that insulin administration 15 min before the meal resulted in better postprandial glycemic control than insulin administration 15 min after the meal (14).

No studies investigated changes in insulin dose for meals of a higher GI. The mismatch between the action of analog insulins and the rapid glucose spike caused by high-GI meals remains a clinical challenge, and practical insulin dosing strategies are needed to address this.

QUESTION 3: WHAT ARE THE IMPLICATIONS FOR CLINICAL PRACTICE?

From the findings of this review, GI, protein, and fat substantially modulate postprandial glucose concentrations in individuals with type 1 diabetes. The impact on 3-h postprandial glucose concentrations of the addition of 35 g fat and 40 g protein to a meal (37) is equivalent to that resulting from the consumption of 20 g carbohydrates without insulin (13). The addition of 50 g fat to a meal can increase insulin requirements by more than twofold (19). This demonstrates that to optimize postprandial glucose control, some mealtime insulin doses need to be adjusted based on the complete meal composition rather than solely on the carbohydrate content.

Whereas meals high in fat and protein require more insulin to control late postprandial hyperglycemia than lower-fat and -protein meals with the same carbohydrate content, as outlined in the previous section, the actual amount of additional insulin and delivery pattern required for high-fat or high-protein meals is not clear. Preliminary studies have indicated that in some individuals, a combo wave bolus extending over 2–2.5 h with as much as a 125% increase in the total insulin dose is required for meals containing 40 g saturated fat (38). As outlined in Fig. 1, an empirical approach is necessary to identify an individual's nutrient sensitivities and optimize insulin dosing for complex meals. As a starting point, initial insulin doses are calculated based on the carbohydrate content of the meal and the individual's CIR, with subsequent incremental dose increases guided by retrospective review of the patient's previous postprandial glucose responses. This review of records can also identify alternative favorite foods with less glycemic effect, and these insights can be helpful in patient education and nutrition counseling.

Of note, in covering higher-fat meals, the amount of insulin given upfront needs to be adjusted to minimize the risk for early postprandial hypoglycemia from delayed gastric emptying induced by the dietary fat. Based on physiological considerations, it seems likely that the percentage of the total insulin dose delivered during the initial phase of a combo wave bolus for higher-fat meals will also need to vary depending on the GI of the meal (more insulin upfront for higher-GI carbohydrate loads). However, as outlined in the previous section, limited scientific data are available regarding the optimal split and duration of the advanced pump boluses for various meal types.

In individuals on multiple dose insulin therapy, strategies frequently suggested in clinical practice for high-fat/low-GI meals (e.g., pizza) are to inject an additional insulin bolus 1 h after the meal to match the delayed absorption

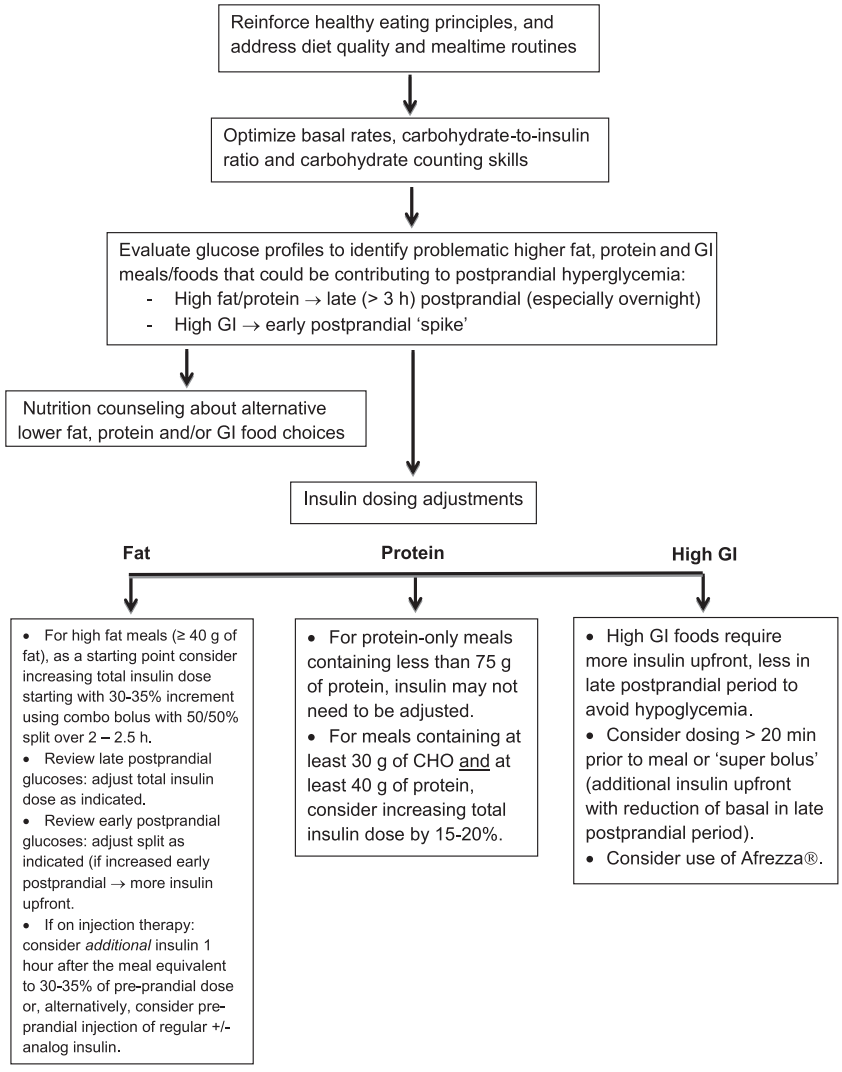

Figure 1—Clinical application of insights about the effects of fat, protein, and GI on postprandial glucose control.

or, alternatively, to cover the meal with a preprandial injection of regular with or without analog insulin. However, these approaches have not been investigated in controlled studies.

Interindividual differences in the impact of macronutrients on postprandial glucose control are another factor compounding the development of standardized insulin dosing algorithms for complex meals (15,19). To date, studies have not been able to identify phenotype markers that correlate with interindividual differences in the glycemic effect of dietary fat. Furthermore, these differences do not appear to correlate with the CIR, and there is no scientific foundation for the use of the CIR as the basis for calculating incremental insulin doses to cover fat [as has been suggested by others (33)].

The mismatch between the rapid glucose absorption following higher-GI meals and the relatively delayed action of subcutaneously administered insulin leads to an initial postprandial glycemic spike that in practice can be difficult to overcome. As indicated in the ADA guidelines, substituting low–glycemic load foods for higher–glycemic load foods may modestly improve glycemic control (2). Increasing the insulin dose to reduce the spike can lead to overinsulinization in the late postprandial period with an associated increased risk for hypoglycemia. Use of a superbolus (an increased insulin bolus upfront followed by basal rate reduction) has been proposed to provide a better match between insulin action and glucose absorption following higher-GI meals. Technosphere insulin (Afrezza), the inhaled prandial insulin recently released in the U.S., has an action profile that may allow for better coverage of higher-GI carbohydrates than insulin analogs delivered subcutaneously (39).

The timing of the insulin dose in relation to the meal is an important factor in optimizing postprandial control. Early delivery of a preprandial insulin bolus for higher-GI carbohydrate loads is another strategy that can be at least partially effective in blunting the initial postprandial spike. In this context, it should be mentioned that unless the individual has gastroparesis, preprandial insulin is preferable to insulin administered during or after the meal for all meal types, including low-GI and high-fat meals.

Finally, clinical education and recommendations should reinforce healthy eating principles and not simply focus on insulin adjustments. In clinical practice, it may be more pertinent to address issues in dietary quality and mealtime routines to improve postprandial control rather than to just focus on fine-tuning mealtime insulin therapy. A registered dietitian can provide a thorough assessment and medical nutrition therapy (1,2).

QUESTION 4: WHAT ARE THE KNOWLEDGE GAPS, AND HOW CAN TECHNOLOGY BE LEVERAGED TO IMPROVE POSTPRANDIAL GLUCOSE CONTROL?

Further research in this area is crucial to provide a stronger evidence base for clinical decision-making. Table 3 outlines some of the issues of practical importance to address in future research. This increased knowledge about the impact of macronutrients on postprandial glucose control and improved insulin dosing algorithms will be of practical relevance only if a pathway for translating the research findings into clinical care is established.

Digital health tools and cloud computing will open opportunities to develop sophisticated analytic systems to automatically evaluate postprandial glucose data and provide dosing recommendations. Carbohydrate counting is a challenging aspect to diabetes self-management, and requiring that fat and protein intake also be quantitated and incorporated in insulin dosing decisions will create an additional burden that few patients will be able to accomplish. The need for both practical simplicity and widespread use of advanced dosing algorithms will ultimately be resolved with the development of data analysis and decision-support tools that evaluate meal patterns to identify whether macronutrients are contributing to glycemic fluctuations and to provide individualized dosing recommendations to patients for their common meals, thereby eliminating the need for patients to routinely count carbohydrates and other macronutrients.

An opportunity exists to capitalize on the control algorithms used in artificial pancreas (AP) technology to optimize current open-loop mealtime insulin dosing. Although AP technology ultimately has the potential to remove any need to calculate insulin dosing, considerable regulatory and technical hurdles must be overcome before an AP system will become a routine tool for the management of type 1 diabetes. Going back almost a decade, methods based on proportional integral derivative control strategies have been used to effect changes in basal insulin delivery with improved fasting glucose control (19,40,41). Metabolic models for predicting future glucose excursions have been developed for use with AP systems (36), and the same approach can be used to analyze postprandial glucose patterns and provide adaptive open-loop bolus dose recommendations (38).

The introduction of continuous glucose monitoring into diabetes care has revealed the complex picture of postprandial glucose patterns in type 1 diabetes, including rapid glucose spikes from higher-GI carbohydrates and late postprandial hyperglycemia from dietary fat and protein, and highlights the limitations of the traditional carbohydrate-based approaches for mealtime insulin dosing. New insights about the effect of dietary macronutrients on postprandial glucose control has been included in the recent ADA standards of medical care, which mention that "for selected individuals. . .the impact

Table 3—Unanswered questions about the effect of dietary fat and protein on postprandial glucose control in type 1 diabetes

How much fat does there need to be in a meal before a clinically significant glycemic effect becomes apparent?
Is there a threshold and/or dose response (i.e., more fat requires more insulin)?
Do all types of fat and protein have similar effects?
Are there phenotypic characteristics that can be used as markers to identify individuals with diabetes who are more nutrient sensitive and will require more insulin to cover higher-fat/protein meals?
What are the optimal insulin dose adjustments needed for common meals with varying fat and protein content?

of protein and fat on glycemic excursions can be incorporated into diabetes management" (1). At a practical level, in reviewing patient glucose records, the possible role of dietary fat and protein as contributors to glycemic fluctuations needs to be considered. Although this review shows that high-fat meals require more insulin coverage than lower-fat meals with identical carbohydrate content and provides some indication of the additional insulin dosages demanded for higher-fat foods (19), we do not yet have simple and easy-to-use insulin dosing algorithms for dietary fat. Ongoing research in conjunction with the development of digital tools to assist patients in dosage decision-making promise solutions to address this need for a better approach to optimizing postprandial insulin coverage that could be readily and widely applied in the management of type 1 diabetes.

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