CHAPTER 1

RATIONALE AND BACKGROUND

Type 2 diabetes mellitus is characterized by abnormal glucose mediated insulin secretion and impaired insulin action in the liver and peripheral tissues, resulting in periods of prolonged hyperglycemia both between meals and immediate post-meal period. Meal and post-meal periods are defines as post-prandial state which cover about two-third of day and is characterized by glucose and other nutrients influx into the blood flow. Following a meal, normal insulin release is rapid and transient. It inhibits hepatic glucose production, promotes hepatic glucose uptake and stimulates peripheral tissues to utilize the nutrient load. Post-prandial hyperglycemia can be an early feature of glucose intolerance and diabetes, reflecting quantitative and/or qualitative abnormalities in insulin secretion by pancreatic beta cells.[1,2] Post-prandial hyperglycemia is also one of the earliest abnormalities of glucose homeostasis associated with type 2 diabetes and is markedly exaggerated in diabetic patients with fasting hyperglycemia.[3]

Individuals with diabetes are at increased risk of developing microvascular complications (e.g. retinopathy, nephropathy, neuropathy), cardiovascular (CHD), and cerebrovascular disease (CVD).[4,5] Several landmark evidences such as the Diabetes Control and Complications Trial (DCCT)[6,7] and United Kingdom Prospective Diabetes Study[8] (UKPDS) demonstrated that improved control of glycemia is associated with a significantly lower risk of the complications of diabetes. In clinical management of diabetes, health care providers usually assess glycemic control with fasting plasma glucose and premeal glucose measurements, as well as measuring HbA_{1c}. Therapeutic goal for HbA_{1c} and fasting/pre-prandial glucose levels have been established.[9] Unfortunately, the majority of patients with diabetes failed to achieve their glycemic goals. Elevated post-prandial glucose concentrations may contribute to this suboptimal glycemic control.

Numerous recent epidemiologic and case-control studies demonstrated that post-prandrial glucose is an independent risk factor for cardiovascular disease in type 2

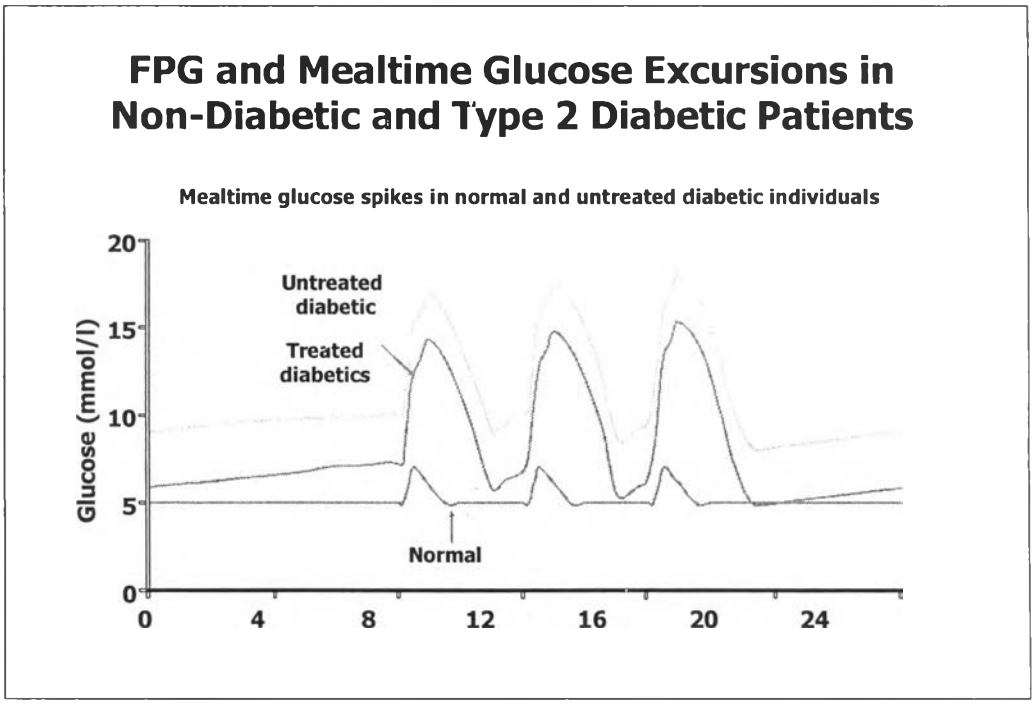

Figure 1 Postprandial hyperglycemia in type 2 diabetes mellitus

diabetes.[10,11,12] Many reports suggested that post-prandial blood glucose may be more predictive of cardiovascular risk than fasting blood glucose.[13,14] It can induce or deteriorate fasting hyperglycemia and be associated with coagulation activation and/or lipid metabolism abnormalities,[15,16] the latter being considered as cardiovascular risk factors, even in non-diabetic populations. Therefore caring for post-prandial glucose regulation is particularly relevant in glucose intolerant and type 2 diabetic patients. Several therapies targeted toward lowering postprandial glucose excursion are now available and have been shown to improve glycemic control as measured by HbA_{1c}.[17,18]

Self-monitoring of blood glucose allows persons who have diabetes to measure their blood glucose levels at home, adjust treatment regimens as needed, and achieve near-normal blood glucose levels. Data from the Diabetes Control and Complications Trial (DCCT), clearly showed that improvement in glycemic control, through intensive insulin therapy and self-monitoring of blood glucose, significantly reduced micro-vascular complications of diabetes[7]. During this trial, patients assigned to intensive therapy monitored blood glucose levels four or more times a day and took insulin by

either multiple daily injections or by continuous subcutaneous insulin infusion using an insulin pump. As a result of the DCCT, self-monitoring of blood glucose levels has become the standard of care for type 1 diabetes mellitus.[19]

In women with diabetes, maintenance of blood glucose levels in the near-normoglycemic range before conception and during pregnancy has been shown to decrease rates of fetal malformation, morbidity, and mortality.[20] Thus SMBG becomes an essential component of any intensive insulin program directed toward achieving near-normoglycemia.

The second Consensus Development Conference on Self-Monitoring of Blood Glucose by the American Diabetes Association (ADA) in 1993 recommended SMBG as an essential component of any intensive insulin program directed toward achieving near-normoglycemia in both type 1 and type 2 diabetes.[21] It is also considered desirable in patients treated with sulfonylureas and in all subjects not achieving glycemic goals. Nevertheless, its role and optimal frequency in type 2 diabetes is still matter of debate, and it has been underlined that its indiscriminate use can cause a waste of resources and psychological harm.

Regardless of the therapy, frequent monitoring is one of the keys to optimal glucose control. A lesser frequency of SMBG may suffice if the patient is still able to secrete substantial amounts of insulin (e.g., recent onset of type 1 DM and most cases of type 2 DM). In these patients glycemic goals often can be met using less complex insulin regimens, oral hypoglycemic agents, and diet. SMBG may be used in these patients to assess temporal patterns (i.e. does glucose concentration rise/fall during the day vs. during the night) so that the morning or evening doses of insulin and/or oral agents can be appropriately increased or decreased. Once therapy is optimized and glycemic control has stabilized, the frequency of monitoring often can be decreased substantially, particularly in people with type 2 diabetes. If the patient's social situation, medical condition, or motivation would discourage or preclude efforts at achieving near-normoglycemia, then the frequency of SMBG or the use of other monitoring systems,

e.g. urine glucose measurements, should be utilized in relation to the patient's willingness or ability to obtain the needed information.

Virtually all intensive therapy programs in insulin-deficient patients depend on the measurement of glucose levels at least four times a day. Knowledge of pre-prandial, bedtime, and nocturnal blood glucose concentrations is required to determine the appropriate basal and pre-prandial insulin doses. The frequency of monitoring usually depends on the patient's current glycemic control. Most people with type 1 diabetes should test four or more times a day to obtain information needed to maintain near-normal levels of blood glucose[22,23,24]. For patients with type 2 diabetes, monitoring can be less intensive if insulin is not part of their medical regimen[25].

It is generally accepted that people using insulin should be provided with guidelines as to how to use SMBG data to appropriately increase their insulin dosage to avoid severe hyperglycemia. However, the value of SMBG is still limited unless it is used as part of an integrated treatment program, constructively modifying their treatment plans in response to the feedback provided by SMBG. For people who use diabetes pills, Self-monitoring is recommended because it may lead to improved blood sugar control and to less frequent episodes of low blood sugar if a person's diet, activity and medications are adjusted based on the monitoring results.

There are some contrast evidences that glycemic control was not consistently influenced by self monitoring of blood or urine. When it was first introduced, home monitoring of blood glucose was claimed to lead to a sustained improvement in glycemic control in insulin dependent diabetes. However, the absence of control groups in many studies has made it impossible to separate the effects of increased education and medical attention from the effects of the blood testing itself. Some studies demonstrated that there was no association between hemoglobin A1c concentration and self monitoring in patients with type 2 diabetes who used insulin[13,15]. It may be that blood glucose monitoring is more effective in true insulin deficiency as opposed to the insulin resistant state or patients with type 2 diabetes might be less familiar with insulin use, more anxious about the risks of cell reserve. It is also important to note that

patients with type 2 diabetes are heterogeneous groups, particularly in terms of pancreatic beta cells reserve, an alternative explanation for the study finding is that self monitoring may be recommended particularly in those patients who are the most difficult to control. More recent studies have suggested that regular self monitoring of blood glucose may be a waste of time for many patients receiving insulin. A comparison of two groups of such patients aged over 40 showed that patients who tested their blood did not have better glycemic control than those who tested their urine, and in a study of young people with insulin dependent diabetes there was no difference in glycemic control between those who tested their blood frequently and those who did not.

The inappropriate use of self monitoring of glucose can be wasteful and can cause psychological harm. Although some patients find that self monitoring enables them to understand and take control of their diabetes, many people with diabetes are performing inaccurate or unnecessary tests. There is no convincing evidence that self monitoring improves glycemic control, nor that blood testing is necessarily better than urine testing. It may be appropriate for some patients not to monitor their own glucose but to rely instead on regular laboratory estimations of glycemic control.

In 2001, approximately 16 million Baht was spent on home monitoring of glucose in Thailand (MIMs, personal communication). Is this enormous cost justified? Is blood testing necessarily better than urine testing? Is glucose self monitoring always necessary, or is it sometimes a waste of time and money? Are recommendations for self monitoring based on sound evidence? What is the optimal frequency of testing? All these questions are needed to be answered.