Depression and Diabetes

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Beginning with early case reports, researchers and clinicians have sought to determine whether diabetes leads to an increased prevalence of psychiatric illnesses. Earlier reviews suggested that the data from such studies were inconclusive and that the design and methods used were inadequate (1). However, over the past several years, a few studies, using more sophisticated methods of case identification and better study designs, have refocused attention on these concerns (2–4). Two papers, a scholarly review in a recent issue of *Diabetes Care* (5) and a study in this issue (this issue, Blanz et al., p. 1579–87) lend support to the idea that diabetes is associated with an increased prevalence of one common psychiatric condition, depression. The issue, whether depression is more common among diabetic patients compared with individuals without diabetes, has several important implications.

First, depression can be a serious, long-term, life-threatening, disabling illness. Depressive disorders often occur during the young-adult years and may persist or recur over long periods of time. Recent studies have documented the social disability associated with depression (6). Some studies suggest that depression may lead to more profound impacts on quality of life than common chronic medical conditions, including diabetes (7). Indeed, our group has found that among patients with type I and type II diabetes, the presence of a psychiatric condition such as major depression is associated with worsened quality of life independent of the severity of diabetes complications (8; A. M. J., M. de Groot, J. Samson, unpublished observations).

Second, depressions are typically very treatable conditions. When properly recognized, considerable and consistent evidence proves that a wide array of psychopharmacological agents and different forms of verbal psychotherapy can ameliorate depressive symptoms and possibly prevent further episodes.

Third, recent studies (3,9) have shown that depression, when present in patients with diabetes, may be associated with worsened glycemic control. The direction of this association is not clear. It is possible that poor glycemic control is a factor in the development of depression, and that the presence of depression leads to altered patient compliance and worsened glycemic control. Indeed, it is reasonable to assume that this is a bidirectional relationship with glycemic control problems and depression affecting each other in reciprocal fashion. Thus, depression may be a risk factor for the progression of the consequences of poor metabolic control, i.e., the microvascular and neuropathic complications of diabetes.

Some investigators (10) have suggested that there may be a special relationship between depression and diabetes because of abnormalities in the hypothalamic-pituitary axis common to both diabetes and depressive disorders. The significance of such endocrinological abnormalities remains unsettled. These abnormalities may be consequences of the neurological and/or metabolic derangement of both disorders. Nonetheless, it is intriguing to speculate about possible underlying endocrinological and neurological pathways that may link depression and diabetes. There may also be other diabetes-specific linkages to depression. For example, irregular blood glucose control, i.e., the rapid shifts between high and low blood glucose levels, could lead to affective lability and therefore depression in genetically at-risk individuals. However, even though many patients describe the mood shifts associated with changes in glucose levels, as yet, no existing evidence suggests that repeated episodes of hypo- or hyperglycemia have a permanent effect on mood disturbance.

Given the lack of evidence about specific neuroendocrine or blood glucose mechanisms linking depression and diabetes, one can reasonably conclude that the increased prevalence of depressive disorder among patients with diabetes is caused by similar factors found in other chronic medical conditions. Furthermore, studies of other chronic disease populations also indicate that depression is more commonly found in these populations than in general populations (11). Thus, the increased prevalence of depression in diabetic populations may not be specific to the diabetic state but rather to the generic effect of the increased stress and strain of having a chronic medical condition. Note that investigators in the diabetes field often limit their attention to differences between diabetic and healthy populations. When comparisons are made between diabetic samples and those with other chronic conditions, such as heart disease or chronic obstructive lung disease, the prevalence rate of depression among di-

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Type I diabetes, insulin-dependent diabetes mellitus; type II diabetes, non-insulin-dependent diabetes mellitus.

abetic patients is not strikingly higher and may be lower than rates found in groups of medically ill patients (11). Further research is needed to address mechanisms linking chronic diseases, including diabetes and development depressive disorder, to firmly draw conclusions about disease-specific versus generic mechanisms of causation.

Although it is reasonable to conclude that evidence from these recent studies of diabetic patients suggests an association with depression, there are still clear limits in the design of most studies. Improved methodology for case assessment has been applied across these studies. However, gathering unbiased samples for accurate comparison of rates of disorder is extraordinarily difficult. Many studies suffer from the problems inherent in trying to gather such true controls for diabetic patients (this issue, Blanz et al., p. 1579–87, 12). This is not an accusation against the researchers, but a reflection of the great difficulty in designing and implementing such studies. It is often the case that samples of convenience are used or samples from diabetic populations in one area are compared with local case registries (this issue, Blanz et al., p. 1579–87) or even data from other communities (12). Rarely do studies gather patients and control subjects in exactly the same manner. There may be considerable, albeit subtle unrecognized biases, inherent when different sampling strategies are used, thereby leading to limitations in conclusions that can be drawn from such studies.

Continuing the careful assessment of hypotheses regarding the effect of diabetes on depression and other psychiatric disorders is clearly necessary. Nonetheless, given the currently available findings from studies such as these cited by Gavard et al. (5) and the work of Blanz et al. (this issue, p. 1579–87), it is reasonable to conclude that diabetic patients, like patients with other chronic medical illnesses, are at increased risk for developing depressive disorders. Thus, an understanding of psychiatric diagnosis and the rudiments of treatment are important clinical skills for the practitioner who sees large numbers of diabetes patients. Yet, considerable evidence from the literature suggests that practitioners of internal medicine, primary care, and family practice frequently under or misdiagnose depressive disorders and, in turn, often undertreat and therefore fail to successfully benefit patients under their care (13,14).

Psychiatric diagnosis depends on old-style medical skills, most importantly a careful history. Although psychiatric problems may seem vague, because no blood depression levels or pathognomic physical findings can be used to ensure a diagnosis or plan a specific treatment, the answers to specific questions can distinguish depression (and its subtypes) from temporary sadness, grief, or anxiety and therefore guide decisions about referral and treatment. Furthermore, one of the most common reasons for treatment failure of depression is an inadequate therapeutic trial with an appropriate antidepressant. Underdosage is often a result of discomfort with diagnosis and inexperience with treatment selection and evaluation. The following clinical vignette underlines this issue—Mr. R. is a 62-year-old man who presented to his internist his increasing fearfulness, thoughts of death, sleeplessness, anxiety, agitation, poor concentration, and a core depressed mood. He was placed on 50 mg of Sertraline and referred for counseling. Two months later, after a few counseling sessions and no further re-evaluation of his psychotropic medications, he self-referred to a psychiatric office where he reported the symptoms as worse. He felt like he was climbing out of his skin and was frightened by his complete personality change. To address his insomnia, he was placed on 15 mg Temazepam at bedtime; to address agitation, he was given Clonazepam 0.5 mg three times a day; and to address his continuing depression, he was increased from the starting dose to 100 mg a day of Sertraline. Within a few days, he was less anxious and sleeping better without needing Temazepam. Over the next several weeks, while being followed biweekly to reassess his response to treatment and to discuss special issues that led to the depression, his depression remitted.

In summary, depression is common in the general population and probably more common among diabetes patients. Thus, a clear understanding of the methods for identification and treatment should be a concern for all clinicians.

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