A recently described protease inactivator matrix (Promogram; Johnson & Johnson, Skipton, U.K.), composed of oxidized regenerated cellulose and collagen, has been shown to reduce elastase, plasmin, and metalloproteinase activity in chronic wound fluids of diabetic patients, stimulating wound repair process (1,2). Both of the components of this matrix, oxidized cellulose (3) and collagen (4), have been reported to accelerate the healing of diabetic foot ulcers.

We assessed the effects of this matrix in two diabetic patients with chronic foot ulcers. G.C., a 76-year-old man with a BMI of 34.9 kg/m^2, type 2 diabetes of 26-year duration, and a previous myocardial infarction, was treated with metformin 2,550 mg/day. HbA_{1c} was 7.5% (upper limit of normal 6.2%). The patient was also affected by hypertension (treated with enalapril and amlodipine) and untreated hypertriglicerydemia and hypercholesterolemia. The patient showed microalbuminuria, with normal creatinine levels, chronic neuropathy with increased vibratory perception threshold bilaterally, peripheral vascular disease (Winsor Index [ankle/arm blood pressure ratio] = 0.75 bilaterally) and a neuroischemic ulcer (3 cm × 4 cm; Wagner grade I) in the plantar region of the right foot. No dry necrolytic tissue was present, and granulation tissue was clearly detectable. Cultural examination of wound fluid did not identify any microorganism, and X-ray was negative for osteomyelitis. Despite standard wound care (surgery curettage and advanced medications) for 24 weeks, the lower-limb lesion did not show any relevant improvement. The matrix was applied twice a week, after the application of polyuretanic foam and hydrobenda. Improvement was noticeable after 3 weeks, with increase of granulation tissue and reduction of wound area. Healing was complete within 5 weeks from the beginning of treatment.

G.I., a 68-year-old woman, was affected by type 2 diabetes with a duration of disease 22 years; her BMI was 25.6 kg/m^2. G.I. was treated with insulin (50 units/day in four administrations), with an HbA_{1c} of 8.0%. She showed signs of neuropathy, with increased vibratory perception thresholds, and peripheral vascular disease (Winsor Index [ankle/arm blood pressure ratio] = 0.70 bilaterally). The patient also reported suboptimally controlled hypertension, chronic renal failure, chronic heart failure, and diabetic retinopathy. She showed an ulcer of the plantar region of the left foot (5 cm × 6 cm) with extensive necrosis, which was surgically removed. Staphylococcus α-hemolytic, *Candida* nonalbicans, and unidentified anaerobial bacteria were isolated from the lesion. For this reason, general treatment with teicoplanin, imipenem, and fluconazole was undertaken, and the infection eradicated within 3 weeks. An X-ray examination of the right foot did not show any sign of osteomyelitis. Despite standard wound care for 40 weeks, the lesion did not heal, although granulation tissue was present. Treatment with oxidized regenerated cellulose and collagen matrix twice a week, after the application of polyuretanic foam and hydrobenda, resulted in a complete healing within 12 weeks.

These two cases suggest that patients suffering from chronic wounds with delayed healing could benefit from this novel treatment, although randomized controlled trials specifically directed at diabetic patients with nonhealing foot ulcers of long duration are needed.

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Assessing the Impact of Diabetes Screening on Quality of Life or Quality of Health?

Semantics are important

Edelman et al. (1) do not, as their title indicates, measure the "impact of screening on quality of life," but rather they measure the effect of screening on health status. Their premise is that it is unclear whether being diagnosed with diabetes might have a potentially detrimental "labeling" effect or whether treatment of previously unrecognized symptoms might improve health-related quality of life (HRQoL). Many important studies, including the U.K. Prospective Diabetes Study (UKPDS) (2), have mistakenly assumed that health status, HRQoL, and quality of life (QoL) are interchangeable terms. However, confusing terminology leads to misinterpreted data and misleading conclusions and titles.

Throughout their article, Edelman et al. recognize the 36-Item Short-Form Health Survey (SF-36) (3) as a health status measure. However, the assumption that health status is synonymous with HRQoL flaws their interpretation. This culminates in their ill-advised conclusion that "early HRQoL changes might not have to be considered in the complex calculations that underlie the decision to undertake or not undertake mass screening for diabetes." From the data presented, it is only evident that changes in perceived health status might not have to be considered.

Bradley (4) has provided a useful commentary on the "importance of differentiating health status from quality of life." Impaired health or well-being may lead to, or be experienced at the same time as impaired quality of life—but not necessarily. Furthermore, excellent health does not infer excellent quality of life. Ware and Sherbourne (3) describe the SF-36 as a health survey but many others treat it, erroneously, as a measure of quality of life.

It is widely acknowledged that the psychological impact of screening for diabetes can vary among individuals, reassuring some and increasing anxiety in

others, although initial distress often wanes over time (5). A more accurate interpretation of the data by Edelman et al. indicates that physical health (measured by the Physical Component Scale) was not affected by undiagnosed diabetes at baseline or by diagnosed diabetes 1 year later. This is unsurprising given that, as the authors acknowledge, complications (which have not been developed yet) and comorbidity are primary determinants of SF-36 scores. However, the controversy regarding screening lies in its impact on mental health, which, in this study, was not affected by undiagnosed diabetes at baseline or by diagnosed diabetes 1 year later. Analysis of the subscales contributing to the Mental Component Scale might provide further insight. "Vitality" might be improved as a result of treating previously undiagnosed symptoms, but improvements might be hidden by deterioration in other subscales, e.g., "mental health."

Edelman et al. present an interesting article about the effects of diabetes screening on health status and discuss several limitations of their study. However, the major criticism of the article concerns their misinterpretation of the data due to the use of misconstrued terminology. Their misleading use of terminology suggests that they have measured the impact of screening on quality of life; in actuality, however, they have only measured the impact of screening on quality of health.

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A Case of Fulminant Type 1 Diabetes With Graves' Disease

Type 1 diabetes is now classified as classic autoimmune (type 1A) and idiopathic (type 1B) diabetes. Fulminant type 1 diabetes was recently characterized as a novel subtype of type 1B diabetes. This disease was characterized as rapid onset, having an absence of diabetes-related autoantibodies, and having the presence of lymphocyte infiltration in exocrine pancreatic tissue without insulitis (1–3). Although fulminant type 1 diabetes has been clinically recognized, its etiology still remains obscure. In this article, we report a case of fulminant type 1 diabetes developed during pregnancy with manifested Graves' disease, which was developed 1 year after onset of diabetes.

A 28-year-old female was admitted to the hospital with diabetic ketoacidosis. She was 27 weeks pregnant and presented no symptom of preceding infection. After admission, she became comatose. Her arterial pH was 6.988 and she had marked elevation of ketone bodies. Her plasma glucose was 43.8 mmol/l; however, her HbA_{1c} was 4.8%. Serum C-peptide was under the detection limit (<0.03 ng/ml), and urinary C-peptide was 0.86 μg/day. There was no response to a glucagon C-peptide stimulation test. Autoantibodies to the cytoplasm of islet, GAD, insulin, and tyrosine phosphate-like protein (IA-2) were all negative. Her serum amylase was 267 IU/l. Both her serum lipase and elastase 1 levels were elevated 55 IU/l and 1,200 ng/dl, respectively. These findings were consistent with symptoms of fulminant type 1 diabetes. Her fetus died, and artificial abortion was performed. The fetus had no superficial abnormality. The subject had HLA-DRB1*0101/*0901, DQB1-*0612/*0306, A2/A24 (9), B7/B61 (40), and Cw7. She was in a euthyroid state, and autoantibodies to the thyroid were negative at that time.

After 1 year she presented overt thyrotoxic symptoms such as hyperhydrosis, palpitation, finger tremor, and poor glycemic control. Her thyroid hormones were elevated, and the thyroid-stimulating hormone receptor antibody was positive. She was diagnosed with Graves' disease and administered propylthiouracil. Her glycemic control was fair with continuous subcutaneous insulin infusion. Diabetes-related autoantibodies were still negative, and her intrinsic insulin secretion was scant. Like a previous short report (4), our case had immunogenetic characteristics of an autoimmune disease except for endocrine pancreas. We often observed classic type 1A diabetes associated with autoimmune thyroid disease. This case was unique in that diabetes developed during pregnancy and was complicated with autoimmune disease. This case may help clarify the etiology of this disease entity.

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