ber of studies showing that nonmydriatic photography and dilated eye examinations are equivalent in screening diabetic retinopathy (i.e., clinical outcomes are very likely to be similar) (3–10). The problem of ungradable photographs in 10–20% of (mostly older) patients can be reduced considerably if the pupils are dilated on a subsequent attempt (8,10). As long as patients with any lesions noted on the photographs are referred to an ophthalmologist, serious problems requiring laser treatment will rarely be missed (9). Thus, less costly nonmydriatic photography is a very reasonable alternative for screening (a camera costs approximately $15,000; assuming a $100 cost for a complete dilated eye examination, the cost of the camera will be met after using it on 150 patients), especially for groups and organizations responsible for the diabetes care of large populations.

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References

1. American Diabetes Association: Management of dyslipidemia in adults with diabetes (Position Statement). *Diabetes Care* 21:179–182, 1998
2. American Diabetes Association: Diabetic retinopathy (Position Statement). *Diabetes Care* 21:157–159, 1998
3. Mohan R, Kohner EM, Aldington SJ, Nijhar I, Mohan V, Mather HM: Evaluation of a non-mydriatic camera in Indian and European diabetic patients. *Br J Ophthalmol* 72:841–845, 1988
4. Weiss H: Validity of routine ophthalmic photography by a non-mydriatic polaroid fundus camera as a screening procedure for early retinal abnormalities in patients with diabetes mellitus. *Pediatr Adolesc Endocrinol* 17:138–146, 1988
5. Jones D, Dolben J, Owens DR, Vora JP, Young S, Creagh FM: Non-mydriatic polaroid photography in screening for diabetic retinopathy: evaluation in a clinical setting. *BMJ* 296:1029–1030, 1988
6. Taylor R, Lovelock L, Michael W, Tunbridge G, George K, Alberti KGMM, Brackenridge RG, Stephenson P, Young E: Comparison of non-mydriatic retinal photography with ophthalmoscopy in 2159 patients: mobile retinal camera study. *BMJ* 301:1243–1247, 1990
7. Leese GP, Newton RW, Jung RT, Haining W, Ellingford A, Tayside Mobile Eye Screening Unit: Screening for diabetic retinopathy in a widely spaced population using non-mydriatic fundus photography in a mobile unit. *Diabet Med* 9:459–462, 1992
8. Lairson DR, Pugh JA, Kapadia AS, Lorimor RJ, Jacobson J, Velez R: Cost-effectiveness of alternative methods for diabetic retinopathy screening. *Diabetes Care* 15:1369–1377, 1992
9. Peters AL, Davidson MB, Ziel FH: Cost-effective screening for diabetic retinopathy using a nonmydriatic retinal camera in a prepaid health-care setting. *Diabetes Care* 16:1193–1195, 1993
10. Pugh JA, Jacobson JM, Van Heuven WAJ, Watters JA, Tuley MR, Lairson DR, Lorimor RJ, Kapadia AS, Velez R: Screening for diabetic retinopathy: the wide angle retinal camera. *Diabetes Care* 16:889–895, 1993

Response to Davidson

Dr. Davidson (1) raises two interesting issues. The first relates to difficulties encountered in implementing guidelines for lipid management when LDL cholesterol cannot be estimated from a simple lipid screen. One option available is a direct measurement of LDL cholesterol. With new methods, this can be obtained for less than $150. As suggested by Dr. Davidson, treatment with a fibrate to lower triglycerides below 400 then reassessing LDL concentration provides a potential alternative in some practice settings. The LDL-based treatment goals suggested by the American Diabetes Association remain tenable, only the approaches to assay LDL cholesterol level differ. Several features of the former approach may make it preferable. First, therapy can be implemented in a more timely manner without requiring exposure of patients to a drug that may not be used for long-term lipid treatment. Second, and perhaps more importantly, it allows ongoing assessment of response to therapy in these patients in whom LDL lowering is found to be necessary. With ever-increasing evidence that long-term LDL lowering affects clinical outcomes in diabetic patients with increased LDL, ongoing measurement of LDL response assumes greater importance.

The second issue raised by Dr. Davidson is again important and practical. These recommendations were not written with a goal of dismissing the utility of the 45° nonmydriatic camera. Rather, they are written to recommend a standard of care. Responsibility (and liability) for both obtaining and interpreting the photographs obtained with the nonmydriatic camera would then reside with the physician (not an eye specialist) supervising the individual obtaining photographs. Some element of standardization in the reading of photographs would be desirable, and issues of conflict of interest regarding use of the diagnostic test for which the physician bills must be addressed. Unless these issues are resolved, it is difficult to endorse the nonmydriatic camera as a "standard of care." Used in the manner suggested by Dr. Davidson, i.e., referring all patients in whom any lesions indicative of retinopathy are noted, would appear to be safe and perhaps decrease patient inconvenience and overall medical cost.

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References

1. Davidson MB: Comments on the position statements "Management of dyslipidemia in adults with diabetes" and "Diabetic retinopathy" (Letter). *Diabetes Care* 21:1378–1379, 1998

Hypoglycemia and Reduction of the Insulin Requirement as a Sign of Celiac Disease in Children With IDDM

It is well known that celiac disease is more frequent in patients with type 1 diabetes than in the general population, but the nonspecific nature of the presenting signs may cause a delay in diagnosis. Thus, Cronin and Shanahan (1) recommend that all IDDM patients should be screened for celiac disease not only at the diagnosis of diabetes, but every few years, since later tests may be positive.

Gillett and Ferguson (2) remark that vague gastrointestinal symptoms and/or anemia may suggest a diagnosis of celiac disease. Increased aminotransferase activity as an early manifestation of celiac disease in IDDM patients, even in the absence of overt gastrointestinal symptoms, has been pointed out by others (3,4). Hypoglycemia as a symptom of celiac disease in diabetic patients has been described in adults (5).

In our center, 24 IDDM patients out of 436 (5.5%) presented celiac disease confirmed by small-bowel biopsy. Of these, 11 patients (45.8%) with an age range from 2 to 16 years and 10 months in a period varying between 2 and 9 months before the diagnosis of celiac disease presented increased frequency of symptomatic hypoglycemia together with a progressive reduction of the insulin requirement (ranging from 30 to 60%) not apparently justified by a reduction of nutrient intake or an increase of physical activity.

Gluten-free dietary treatment induced in all cases an increase in insulin requirement up to the doses usually administered in diabetic patients without celiac disease matched for age, sex, and duration of IDDM.

The spontaneous reintroduction of gluten in two patients with poor compliance to the diet was immediately followed by a sharp reduction in the insulin requirement in both cases and by a severe hypoglycemic crisis in one of the two. This happened after 28 and 32 months of diet therapy, respectively.

In conclusion, hypoglycemia with a consequent reduction of the insulin requirement seems to be a valid sign of active celiac disease in patients with diabetes and of poor compliance to the gluten-free diet in patients already diagnosed.

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References

1. Cronin CC, Shanahan F: Insulin-dependent diabetes mellitus and coeliac disease. *Lancet* 349:1096–1097, 1997
2. Gillett HR, Ferguson A: Coeliac disease and insulin-dependent diabetes mellitus (Letter). *Lancet* 349:1698, 1997
3. Vajro P, Fontanella A, Mayer M, De Vincenzo A, Terracciano LM, D'Armiento M, Vecchione R: Elevated serum aminotransferase activity as an early manifestation of gluten-sensitive enteropathy. *J Pediatr* 122:416–419, 1993
4. Lorini R, Maggiore G, De Giacomo C, Vitali L: Elevated serum aminotransferase activity: an early manifestation of gluten-sensitive enteropathy in children with insulin dependent diabetes mellitus (Letter). *J Pediatr* 124:995, 1994
5. Walsh CH, Cooper BT, Wright AD, Malins JM, Cooke WT: Diabetes mellitus and coeliac disease: a clinical study. *QFM* 47:89–100, 1978

Response to Iafusco et al.

Coexistence of celiac disease in patients with IDDM

A relationship between celiac disease (CD) and IDDM has been recognized for 30 years (1-5). Thain et al. (6) reviewed data on six children (10 months to 15 years) with coexisting CD and IDDM in 1974, and Walsh et al. (7) published a thorough clinical study of 14 adults with IDDM and CD in 1978. The authors of both reviews stressed that malabsorption was suggested in patients with IDDM by problems with glucose control, particularly diminishing insulin requirements and frequent hypoglycemic reactions. In virtually all patients, the IDDM was diagnosed before the CD. All 6 of the children reported by Thain et al. and 13 of 14 patients reviewed by Walsh et al. had gastrointestinal symptoms/signs consistent with a malabsorption syndrome, and the diagnosis of CD was established by peroral small intestinal biopsies.

The coexistence of these diseases appears to be due to a common genetic predisposition. Susceptibility to both has been localized to the HLA region on chromosome 6 (8). Studies performed by Hitman et al. (8) revealed that 63% of 79 patients with IDDM and 89% of 46 patients with CD were HLA DR3 positive. Only 32% of 161 control subjects were positive for this HLA II antigen.

The true incidence of CD in patients with IDDM was impossible to estimate until a sensitive and specific serologic test for CD was developed. This became possible with the development of the immunoglobulin (Ig) A–endomysial antibody test (EMA-IgA). This test has been refined to a point at which it is virtually 100% sensitive and specific for diagnosis of untreated CD when it is performed in an established reference laboratory (9). Endomysial antibodies of the IgA subclass present in serum bind to the reticulin component of the endomysium of the smooth muscle of monkey esophagus, and the substrate-bound IgA antibody can be detected by immunofluorescence (10). Rossi et al. (11) studied 211 children with IDDM followed in the endocrinology clinic at Children's Hospital in Buffalo, New York, during 1986–1987 and found EMA-IgA in 10, for an incidence of 4.7%. None had gastrointestinal symptoms. Talal et al. (12) screened 185 adult patients with IDDM who were managed by the diabetologists at the University of Iowa Hospitals and Clinics (Iowa City, IA) for EMA-IgA and detected a positive titer in 9 (4.8%). Gastrointestinal symptoms reported by the entire population of patients with IDDM included diarrhea (28.1%), constipation (27.5%), early satiety (22.7%), dyspepsia (23.2%), steatorrhea (17.2%), and symptoms consistent with lactose intolerance (10.8%). The only symptom that was significantly associated with EMA-IgA positivity was lactose intolerance ($P < 0.005$). Both groups of investigators recommended screening of all patients with IDDM for CD with EMA-IgA. There would be a significant negative cost if the entire population were to be screened, in light of the fact that <5% of patients will have a positive titer. Further, a negative antibody titer at one point in time does not exclude development of symptomatic CD in the future. EMA-IgA is more expensive than other screening tests for CD (e.g., antigliadin IgG and IgA), but this is offset by extremely high positive- and negative-predictive values. Costs relate to the fact that monkey esophagus is used. Cronin et al. (13) screened 101 adults with IDDM (aged 18–59 years) with EMA-IgA measured by indirect immunofluorescence using sections of umbilical cord rather than monkey esophagus. Eight of these Irish patients tested positive for the antibody (7.9%). Substitution of human umbilical cord for monkey esophagus will reduce the cost of the test.

Iafusco and coworkers from Naples, Italy, report their observations on the devel-