During GE scintigraphy, postprandial scans at 1 hour can identify accelerated GE, while scans at 2 and 4 hours distinguish normal function from delayed GE with a sensitivity of 90% and a specificity of 70% (40). For solid-phase testing, most centers use a 99mTc sulfur colloid-labeled egg sandwich as the test meal, with imaging at 0, 1, 2, and 4 hours. The Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society recommend a 4-hour test using a radiolabeled EggBeaters® meal with jam, toast, and water (41). Sometimes there is a discrepancy between test results, i.e., patients have retained food at endoscopy but normal GE by scintigraphy. This discrepancy may be explained by day-to-day variations in GE, the use of medications (e.g., opioids) that can delay GE before either study, ingestion of food before an endoscopy, or differences between the gastric motor mechanisms responsible for antral motility and emptying of smaller particles during scintigraphy (i.e., type 2 antral motor activity) and indigestible larger particles (i.e., ≥3 mm size) ingested with meals, which are emptied by the antral component of the migrating motor complex during fasting or sleeping.

Gastric emptying breath tests (GEBT) offer an alternative approach for measuring solid phase GE. The meal includes *Spirulina platensis* or the medium chain triglyceride octanoate enriched with ^{13}C, which is a stable isotope. After GE and duodenal digestion, ^{13}C is released from the substrate, exhaled, and measured by isotope ratio mass spectrometry, allowing GE $t_{1/2}$ to be calculated (42,43,44). In contrast to scintigraphy, GEBT does not require elaborate detection equipment or entail radiation exposure and can be performed at the point of care, as in the office or bedside, because the collected breath samples are collected simply with a straw and sealable container, and the excreted $^{13}CO_2$ is stable. A ^{13}C-spirulina GEBT has been approved for use in the United States by the Food and Drug Administration.

GE can also be measured by a nondigestible capsule, SmartPill® wireless motility capsule, which records luminal pH, temperature, and pressure during GI transit, providing a measure of GE time. In the pivotal study, GE measured by a capsule and by scintigraphy at 4 hours were significantly correlated with a coefficient of 0.73 (45). Compared to scintigraphic emptying at 4 hours, the capsule had 86% sensitivity and 92% specificity for diagnosing gastroparesis. After initial testing to identify disturbances of transit, more detailed testing with intraluminal techniques (i.e., antropyloroduodenojejunal manometry) may be useful for characterizing motor dysfunctions and guiding therapy (16). Autonomic function tests are useful for identifying autonomic dysfunctions (e.g., vagal neuropathy) that are associated with gastroparesis. Reduced variability of the cardiac RR interval provides a simple screening assessment of vagal dysfunction (46).

Management. The principles of gastroparesis management are to address fluid and nutritional requirements, improve glycemic control, and treat symptoms. These measures have been summarized in guidelines (47).

Diarrhea

Definition. Diabetic diarrhea is defined by loose and frequent stools, generally more than three bowel movements daily in patients with diabetes.

Epidemiology. Some, but not all, population-based studies, which have been exclusively based on type 2 diabetes (4,5) or combined both patients with type 1 diabetes and type 2 diabetes (8), reported a higher prevalence of diarrhea in patients with diabetes than in nondiabetic controls (Table 27.1). For example, in a sample of 423 patients with predominantly (95%) type 2 diabetes, 15.6% reported diarrhea or constipation versus 10% of nondiabetic controls (4). A systematic review of all English-language observational studies and trials from inception through April 2010 highlighted the known link between metformin and diarrhea (48). For example, among 5,021 participants in five randomized controlled trials, the incidence of diarrhea was higher for subjects treated with metformin (15%–24%) than for those treated with thiazolidinediones (3%–8%) (48). Likewise, the incidence was higher for metformin (2.5%–50%) than for sulfonylureas (0%–13%) treatment (48). No systematic assessments have been conducted of the clinical features, risk factors, or natural history of diabetic diarrhea.

Diagnostic Tests. If diarrhea cannot be attributed to metformin or ingestion of incompletely absorbed carbohydrates, further assessment should be considered, particularly in type 1 diabetes. Drugs used in diabetes may also result in diarrhea (49). The association between type 1 diabetes and CD is considered separately in this chapter. A 24-hour stool collection to quantify stool weight and fat content should be performed to identify fat malabsorption. While CD and bacterial overgrowth can cause malabsorption, testing for these conditions should be considered even when stool examination does not reveal malabsorption. A duodenal aspirate to assess for bacterial overgrowth and duodenal biopsies to exclude CD can be obtained at upper GI endoscopy. While lactulose or glucose hydrogen breath tests are widely used to identify bacterial overgrowth, their use is limited, since rapid delivery of the substrate to the colon can also give rise to an early breath hydrogen peak (50).

Management. Diabetic diarrhea is treated symptomatically with loperamide, preferably administered 30 minutes before meals, in the dose range of 2–16 mg per day. Consumption of artificial sweeteners that contain the osmotically active sugar substitute sorbitol should be reduced. Second line approaches are clonidine, 0.1 mg orally (51) or by patch in patients who do not experience significant postural hypotension. Amitriptyline, which has anticholinergic effects, may reduce intestinal cramping and transit. Octreotide (25–50 µg subcutaneously 5–10 minutes before meals) delays small intestinal transit (52) and may also reduce secretory diarrhea associated with rapid intestinal transit

TABLE 27.13. Growth and Glycemic Control in Patients With Type 1 Diabetes With Treatment of Celiac Disease

LOCATION, YEARS (REF.)	NUMBER OF PATIENTS STUDIED	GROWTH AT DIAGNOSIS OF CD		EFFECT OF GFD ON GROWTH		GLYCEMIC CONTROL (A1C)	
		Weight	Height	Weight	Height	At Diagnosis	On a GFD
Finland, 1994–1999 (150)	18	↓	→	↑	→	→	→
Germany, Austria, 1985–2002 (161)	127	↓	↓	→	→	↓	→
Australia, 1989–1999 (156)	21	↓	↓	↑	→	-----	→
Denmark, 1997, 2002–2003 (152)	28	↓	↓	↑	↑	→	→
United States, NR (112)	30	↓	→	↑	↑	-----	-----
United Kingdom, 1998–2006 (145)	22	→	-----	↑	→	-----	-----
Austria, Germany, 1995–2009 (162)	183	↓	↓	→	→	→	→
Israel, 1983–2008 (153)	68	→	→	→	→	→	→
Germany, 1994–1999 (151)	9	→	→	→	↑	→	→
Australia, 1990–2010 (163)	129	-----	-----	-----	-----	↓	↓*

↓, decreased; →, no change; ↑, increased; -----, no data; A1c, glycosylated hemoglobin; CD, celiac disease; GFD, gluten-free diet; NR, not reported.
* Compared to those nonadherent to a GFD.

SOURCE: References are listed within the table.

These conditions are associated with inflammatory injury of usually the distal small intestine and/or colon. Ulcerative colitis only affects the large intestine. IBD and type 1 diabetes share some genetic predispositions (120). Despite that, there is only a weak positive association between ulcerative colitis and type 1 diabetes, and in particular, this is seen for pediatric IBD. The odds ratio for diabetes in pediatric-onset IBD is 2.7 (95% CI 1.1–6.6) (121). In two larger datasets, the IMS Health Integrated Queens Database and the Market Scan Commercial Claims and Encounters Database, no association was seen between IBD and type 1 diabetes (122). A secondary association was reported from the Multigeneration Registry Study in Sweden showing that the risk of type 1 diabetes was increased modestly in offspring of parents with ulcerative colitis with a standardized incidence ratio of 1.23, though this was less than that of CD at 2.73 (123).

The treatment, especially for ulcerative colitis, often is based on the use of corticosteroids. Studies that report the development of diabetes in patients with ulcerative colitis generally have little data measuring the actual risk. While it is well recognized that the chronic use of corticosteroids substantially increases the risk of diabetes, there are relatively few case-control studies and very few data for patients with IBD. In one case-control series of 55 adult patients with active Crohn's disease, treatment with systemic corticosteroids substantially increased the risk of hyperglycemia (124), though the confidence intervals overlapped 1.0. There are very few data regarding the risk of diabetes in patients with IBD treated with corticosteroids.

AUTOIMMUNE GASTRITIS

Autoimmune gastritis can also be associated with type 1 diabetes because of a common genetic background or tendency to autoimmunity (125,126). Autoimmune gastritis is a T cell-mediated disease marked by the presence of autoantibodies directed against the H+/K+ ATPase in the parietal cells of the stomach. This tissue-specific autoimmunity can result in reduction of acid production in the stomach, hypochlorhydria, and iron deficiency. The gastric mucosa can become atrophic. Consequent to the loss of ability of the parietal cells to produce acid, the neuroendocrine cells of the stomach reduce the negative regulation that is exerted by the acid pH via somatostatin, thereby leading to unrestrained gastrin secretion. Hypergastrinemia may be seen in 7% of patients with type 1 diabetes (127). Vitamin B12 deficiency is uncommon, though it can occur in patients with markers for pernicious anemia (127).

This hypersecretion of gastrin leads to hypertrophy of enterochromaffin cells in the stomach, which in turn can lead to carcinoid development (128). The loss of parietal cell mass leads to reduced digestive acid that is needed for effective cleavage of vitamin B12 from food sources and also reduces intrinsic factor production. Both lead to vitamin B12 deficiency (i.e., pernicious anemia) (125). The acid-producing cells of the stomach also produce pepsinogen, which is activated by low pH to aid in digestion.

Diagnosis

Atrophic gastritis can be detected by the identification of parietal cell antibodies (PCAs) or, more recently, the ATP4A autoantibody (129) in the serum, low serum pepsinogen I, the demonstration of atrophy of the gastric body mucosa on endoscopic biopsies, and often by very high levels of gastrin in the fasting state. Autoantibodies may exist long before the results of loss of parietal cell mass and function become apparent in the form of iron and vitamin B12 deficiency. While noninvasive tests may suggest atrophic gastritis, biopsies are needed for confirmation and to distinguish from other forms of gastritis. Other consequences, such as small intestinal bacteria overgrowth and calcium malabsorption, may also occur.

Autoimmune Gastritis in Type 1 Diabetes

Several cross-sectional studies have documented a three to five times increased prevalence of autoimmune gastritis in patients with type 1 diabetes compared with healthy controls from the general population (Table 27.14). Much less data are available on the natural history of autoimmune gastritis in type 1 diabetes (127), however, suggesting that many patients with PCA may not progress to parietal cell organ failure. Pernicious anemia, the classic endpoint of autoimmune gastritis, may take years or decades to become evident.

Duration of diabetes, independent of age, does not appear to be associated with likelihood of atrophic gastritis. Females have somewhat greater risk than males, though studies do not always agree. African Americans seem to be equally likely to have PCA as whites (130).

TABLE 27.14. Epidemiologic Studies of Autoimmune Gastritis in Type 1 Diabetes

LOCATION, YEARS (REF.)	STUDY POPULATION	NUMBER IN STUDY	PARIETAL CELL ANTIBODY	KEY FINDINGS
United States				
NR (164)	Referral population with type 1 diabetes (age 2–30 years)	771	9% PCA positive, F>M	6/11 PCA positive had achlorhydria
NR (165)	Cohort children	211	10 PCA positive, 3/4 biopsied	
NR (130)	Consecutive cohort children and adults	1,696	186 PCA positive (11%)	Equal in blacks; slight female predominance
Europe and rest of world				
Finland, NR (166)	Referral population, diabetic children	147	8 PCA positive	Hypochlorhydria
Belgium, 1998–2000 (126)	Community cohort, adults	229	69 PCA positive	Associated with *H. pylori*, HLA, hypergastrinemia, iron deficient anemia
United Kingdom, NR (167)	Children and adults	366	48 PCA positive	Mixed group
Spain, 2001–2006 (127)	Cohort adults	168	44 PCA positive	11 also had low PI, 96% DQ2

DQ2 is defined by the carriage of the gene pair DQA1:05.DQB1:02. HLA, human leukocyte antigen; NR, not reported; PCA, parietal cell antibody; PI, pepsinogen I.

SOURCE: References are listed within the table.

LIST OF ABBREVIATIONS

A1c. . . . . .glycosylated hemoglobin
CD . . . . . .celiac disease
CI. . . . . .confidence interval
GE . . . . . .gastric emptying
GEBT . . . . . .gastric emptying breath tests
GFD . . . . . .gluten-free diet
GI. . . . . .gastrointestinal
HLA . . . . . .human leukocyte antigen
HR . . . . . .hazard ratio
IBD . . . . . .inflammatory bowel disease
IDR. . . . . .incident death rate
IgA. . . . . .immunoglobulin A
IgG. . . . . .immunoglobulin G
LADA . . . . . .latent autoimmune diabetes of adults
PCA . . . . . .parietal cell antibody
TTG . . . . . .tissue transglutaminase

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CONVERSIONS

Conversions for glucose values are provided in *Diabetes in America Appendix 1 Conversions*.

DUALITY OF INTEREST

Drs. Bharucha, Locke, and Murray reported no conflicts of interest.

REFERENCES

1. Everhart JE: Digestive diseases and diabetes. In *Diabetes in America*. 2nd ed. Harris MI, Cowie CC, Stern MP, Boyko EJ, Reiber GE, Bennett PH, Eds. Bethesda, MD, National Institutes of Health, NIH Pub No. 95-1468, 1995, p. 457–483
2. Noel RA, Braun DK, Patterson RE, Bloomgren GL: Increased risk of acute pancreatitis and biliary disease observed in patients with type 2 diabetes: a retrospective cohort study. *Diabetes Care* 32:834–838, 2009
3. Melton LJ 3rd: History of the Rochester Epidemiology Project. *Mayo Clin Proc* 71:266–274, 1996
4. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M: Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15,000 adults. *Arch Intern Med* 161:1989–1996, 2001
5. Hammer J, Howell S, Bytzer P, Horowitz M, Talley NJ: Symptom clustering in subjects with and without diabetes mellitus: a population-based study of 15,000 Australian adults. *Am J Gastroenterol* 98:391–398, 2003
6. Talley NJ, Howell S, Jones MP, Horowitz M: Predictors of turnover of lower gastrointestinal symptoms in diabetes mellitus. *Am J Gastroenterol* 97:3087–3094, 2002
7. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, Wilson DM, O'Brien PC, Melton LJ 3rd, Service FJ: The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. *Neurology* 43:817–824, 1993
8. Maleki D, Locke GR 3rd, Camilleri M, Zinsmeister AR, Yawn BP, Leibson C, Melton LJ 3rd: Gastrointestinal tract symptoms among persons with diabetes mellitus in the community. *Arch Intern Med* 160:2808–2816, 2000
9. Janatuinen E, Pikkarainen P, Laakso M, Pyorala K: Gastrointestinal symptoms in middle-aged diabetic patients. *Scand J Gastroenterol* 28:427–432, 1993
10. Lovell RM, Ford AC: Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clin Gastroenterol Hepatol* 10:712–721.e4, 2012
11. Ordog T: Interstitial cells of Cajal in diabetic gastroenteropathy. *Neurogastroenterol Motil* 20:8–18, 2008
12. Chandrasekharan B, Srinivasan S: Diabetes and the enteric nervous system. *Neurogastroenterol Motil* 19:951–960, 2007
13. de Kort S, Kruimel JW, Sels JP, Arts IC, Schaper NC, Masclee AA: Gastrointestinal symptoms in diabetes mellitus, and their relation to anxiety and depression. *Diabetes Res Clin Pract* 96:248–255, 2012
14. Hasler WL, Parkman HP, Wilson LA, Pasricha PJ, Koch KL, Abell TL, Snape WJ, Farrugia G, Lee L, Tonascia J, Unalp-Arida A, Hamilton F; NIDDK Gastroparesis Clinical Research Consortium: Psychological dysfunction is associated with symptom severity but not disease etiology or degree of gastric retention in patients with gastroparesis. *Am J Gastroenterol* 105:2357–2367, 2010
15. Hasler WL, Wilson LA, Parkman HP, Koch KL, Abell TL, Nguyen L, Pasricha PJ, Snape WJ, McCallum RW, Sarosiek I, Farrugia G, Calles J, Lee L, Tonascia J, Unalp-Arida A, Hamilton F: Factors related to abdominal pain in gastroparesis: contrast to patients with predominant nausea and vomiting. *Neurogastroenterol Motil* 25:427–438, e300–e301, 2013
16. Camilleri M: Gastrointestinal problems in diabetes. *Endocrinol Metab Clin North Am* 25:361–378, 1996
17. Feldman M, Corbett DB, Ramsey EJ, Walsh JH, Richardson CT: Abnormal gastric function in longstanding, insulin-dependent diabetic patients. *Gastroenterology* 77:12–17, 1979
18. Samsom M, Salet GA, Roelofs JM, Akkermans LM, Vanberge-Henegouwen GP, Smout AJ: Compliance of the proximal stomach and dyspeptic symptoms in patients with type I diabetes mellitus. *Dig Dis Sci* 40:2037–2042, 1995
19. Camilleri M, Malagelada JR: Abnormal intestinal motility in diabetics with the gastroparesis syndrome. *Eur J Clin Invest* 14:420–427, 1984
20. Barnett JL, Owyang C: Serum glucose concentration as a modulator of interdigestive gastric motility. *Gastroenterology* 94:739–744, 1988
21. Hasler WL, Soudah HC, Dulai G, Owyang C: Mediation of hyperglycemia-evoked gastric slow-wave dysrhythmias by endogenous prostaglandins. *Gastroenterology* 108:727–736, 1995
22. Samsom M, Akkermans LM, Jebbink RJ, van Isselt H, vanBerge-Henegouwen GP, Smout AJ: Gastrointestinal motor mechanisms in hyperglycaemia induced delayed gastric emptying in type I diabetes mellitus. *Gut* 40:641–646, 1997
23. MacGregor IL, Gueller R, Watts HD, Meyer JH: The effect of acute hyperglycemia on gastric emptying in man. *Gastroenterology* 70:190–196, 1976
24. Fraser RJ, Horowitz M, Maddox AF, Harding PE, Chatterton BE, Dent J: Hyperglycaemia slows gastric emptying in type 1 (insulin-dependent) diabetes mellitus. *Diabetologia* 33:675–680, 1990
25. Oster-Jorgensen E, Pedersen SA, Larsen ML: The influence of induced hyperglycaemia on gastric emptying rate in healthy humans. *Scand J Clin Lab Invest* 50:831–836, 1990
26. Schvarcz E, Palmer M, Aman J, Horowitz M, Stridsberg M, Berne C: Physiological hyperglycemia slows gastric emptying in normal subjects and patients with insulin-dependent diabetes mellitus. *Gastroenterology* 113:60–66, 1997
27. Colwell JA: Intensive insulin therapy in type II diabetes: rationale and collaborative clinical trial results. *Diabetes* 45(Suppl 3):S87–S90, 1996
28. Vella A, Lee JS, Camilleri M, Szarka LA, Burton DD, Zinsmeister AR, Rizza RA, Klein PD: Effects of pramlintide, an amylin analogue, on gastric emptying in type 1 and 2 diabetes mellitus. *Neurogastroenterol Motil* 14:123–131, 2002
29. Schirra J, Leicht P, Hildebrand P, Beglinger C, Arnold R, Goke B, Katschinski M: Mechanisms of the antidiabetic action of subcutaneous glucagon-like peptide-1(7-36)amide in non-insulin dependent diabetes mellitus. *J Endocrinol* 156:177–186, 1998
30. Zander M, Madsbad S, Madsen JL, Holst JJ: Effect of 6-week course of glucagon-like peptide 1 on glycaemic control, insulin sensitivity, and beta-cell function in type 2 diabetes: a parallel-group study. *Lancet* 359:824–830, 2002
31. Choung RS, Locke GR 3rd, Schleck CD, Zinsmeister AR, Melton LJ 3rd, Talley NJ: Risk of gastroparesis in subjects with type 1 and 2 diabetes in the general population. *Am J Gastroenterol* 107:82–88, 2012

32. Quan C, Talley NJ, Jones MP, Spies J, Horowitz M: Gain and loss of gastrointestinal symptoms in diabetes mellitus: associations with psychiatric disease, glycemic control, and autonomic neuropathy over 2 years of follow-up. *Am J Gastroenterol* 103:2023–2030, 2008
33. Talley NJ, Young L, Bytzer P, Hammer J, Leemon M, Jones M, Horowitz M: Impact of chronic gastrointestinal symptoms in diabetes mellitus on health-related quality of life. *Am J Gastroenterol* 96:71–76, 2001
34. Jones KL, Russo A, Berry MK, Stevens JE, Wishart JM, Horowitz M: A longitudinal study of gastric emptying and upper gastrointestinal symptoms in patients with diabetes mellitus. *Am J Med* 113:449–455, 2002
35. Chang J, Russo A, Bound M, Rayner CK, Jones KL, Horowitz M: A 25-year longitudinal evaluation of gastric emptying in diabetes. *Diabetes Care* 35:2594–2596, 2012
36. Kong MF, Horowitz M, Jones KL, Wishart JM, Harding PE: Natural history of diabetic gastroparesis. *Diabetes Care* 22:503–507, 1999
37. Hyett B, Martinez FJ, Gill BM, Mehra S, Lembo A, Kelly CP, Leffler DA: Delayed radionucleotide gastric emptying studies predict morbidity in diabetics with symptoms of gastroparesis. *Gastroenterology* 137:445–452, 2009
38. Pasricha PJ, Yates KP, Clarke JO, Unalp A, Tonascia J, Koch KL, Hasler WL, Miriel LA, Abell TL, Snape WJ, Calles J, McCallum RW, Sarosiek I, Hamilton FA, Farrugia G, Nguyen L, Parkman HP; GpCRC Consortium: Mortality and predictors of improvement in patients with gastroparesis: 4-year outcomes from the Gastroparesis Clinical Research Consortium. *Gastroenterology* 146(Suppl 1):S-136, 2014
39. Chang J, Rayner CK, Jones KL, Horowitz M: Diabetic gastroparesis and its impact on glycemia. *Endocrinol Metab Clin North Am* 39:745–762, 2010
40. Camilleri M, Zinsmeister AR, Greydanus MP, Brown ML, Proano M: Towards a less costly but accurate test of gastric emptying and small bowel transit. *Dig Dis Sci* 36:609–615, 1991
41. Abell TL, Camilleri M, Donohoe K, Hasler WL, Lin HC, Maurer AH, McCallum RW, Nowak T, Nusynowitz ML, Parkman HP, Shreve P, Szarka LA, Snape WJ, Jr., Ziessman HA; American Neurogastroenterology and Motility Society; Society of Nuclear Medicine: Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol* 103:753–763, 2008
42. Szarka LA, Camilleri M, Vella A, Burton D, Baxter K, Simonson J, Zinsmeister AR: A stable isotope breath test with a standard meal for abnormal gastric emptying solids in the clinic and in research. *Clin Gastroenterol Hepatol* 6:635–643, 2008
43. Bharucha AE, Camilleri M, Veil E, Burton D, Zinsmeister AR: Comprehensive assessment of gastric emptying with a stable isotope breath test. *Neurogastroenterol Motil* 25:e60–e69, 2013
44. Ziegler D, Schadewaldt P, Pour Mirza A, Piolot R, Schommartz B, Reinhardt M, Vosberg H, Brosicke H, Gries FA: [13C]octanoic acid breath test for non-invasive assessment of gastric emptying in diabetic patients: validation and relationship to gastric symptoms and cardiovascular autonomic function. *Diabetologia* 39:823–830, 1996
45. Kuo B, McCallum RW, Koch KL, Sitrin MD, Wo JM, Chey WD, Hasler WL, Lackner JM, Katz LA, Semler JR, Wilding GE, Parkman HP: Comparison of gastric emptying of a nondigestible capsule to a radio-labelled meal in healthy and gastroparetic subjects. *Aliment Pharmacol Ther* 27:186–196, 2008
46. Bharucha AE, Camilleri M, Low PA, Zinsmeister AR: Autonomic dysfunction in gastrointestinal motility disorders. *Gut* 34:397–401, 1993
47. Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L; American College of Gastroenterology: Clinical guideline: management of gastroparesis. *Am J Gastroenterol* 108:18–37, 2013
48. Bennett WL, Maruthur NM, Singh S, Segal JB, Wilson LM, Chatterjee R, Marinopoulos SS, Puhan MA, Ranasinghe P, Block L, Nicholson WK, Hutfless S, Bass EB, Bolen S: Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. *Ann Intern Med* 154:602–613, 2011
49. Rubio-Tapia A, Herman ML, Ludvigsson JF, Kelly DG, Mangan TF, Wu TT, Murray JA: Severe spruelike enteropathy associated with olmesartan. *Mayo Clin Proc* 87:732–738, 2012
50. Posserud I, Stotzer PO, Bjornsson ES, Abrahamsson H, Simren M: Small intestinal bacterial overgrowth in patients with irritable bowel syndrome. *Gut* 56:802–808, 2007
51. Fedorak RN, Field M, Chang EB: Treatment of diabetic diarrhea with clonidine. *Ann Intern Med* 102:197–199, 1985
52. von der Ohe MR, Camilleri M, Thomforde GM, Klee GG: Differential regional effects of octreotide on human gastrointestinal motor function. *Gut* 36:743–748, 1995
53. Mourad FH, Gorard D, Thillainayagam AV, Colin-Jones D, Farthing MJ: Effective treatment of diabetic diarrhoea with somatostatin analogue, octreotide. *Gut* 33:1578–1580, 1992
54. Soudah HC, Hasler WL, Owyang C: Effect of octreotide on intestinal motility and bacterial overgrowth in scleroderma. *N Engl J Med* 325:1461–1467, 1991
55. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC: Functional bowel disorders. *Gastroenterology* 130:1480–1491, 2006
56. Maleki D, Camilleri M, Burton DD, Rath-Harvey DM, Oenning L, Pemberton JH, Low PA: Pilot study of pathophysiology of constipation among community diabetics. *Dig Dis Sci* 43:2373–2378, 1998
57. Battle WM, Snape WJ, Jr., Alavi A, Cohen S, Braunstein S: Colonic dysfunction in diabetes mellitus. *Gastroenterology* 79:1217–1221, 1980
58. Sims MA, Hasler WL, Chey WD, Kim MS, Owyang C: Hyperglycemia inhibits mechanoreceptor-mediated gastrocolonic responses and colonic peristaltic reflexes in healthy humans. *Gastroenterology* 108:350–359, 1995
59. Maleki D, Camilleri M, Zinsmeister AR, Rizza RA: Effect of acute hyperglycemia on colorectal motor and sensory function in humans. *Am J Physiol* 273:G859–G864, 1997
60. Bharucha AE, Pemberton JH, Locke GR 3rd: American Gastroenterological Association technical review on constipation. *Gastroenterology* 144:218–238, 2013
61. Bharucha AE, Low P, Camilleri M, Veil E, Burton D, Kudva Y, Shah P, Gehrking T, Zinsmeister AR: A randomised controlled study of the effect of cholinesterase inhibition on colon function in patients with diabetes mellitus and constipation. *Gut* 62:708–715, 2013

62. Bharucha AE, Dorn SD, Lembo A, Pressman A: American Gastroenterological Association medical position statement on constipation. *Gastroenterology* 144:211–217, 2013
63. Ascaso JF, Herreros B, Sanchiz V, Lluch I, Real JT, Minguez M, Mora F, Benages A: Oesophageal motility disorders in type 1 diabetes mellitus and their relation to cardiovascular autonomic neuropathy. *Neurogastroenterol Motil* 18:813–822, 2006
64. Kinekawa F, Kubo F, Matsuda K, Kobayashi M, Furuta Y, Fujita Y, Okada H, Muraoka T, Yamanouchi H, Inoue H, Uchida Y, Masaki T: Esophageal function worsens with long duration of diabetes. *J Gastroenterol* 43:338–344, 2008
65. Lee SD, Keum B, Chun HJ, Bak YT: Gastroesophageal reflux disease in type II diabetes mellitus with or without peripheral neuropathy. *J Neurogastroenterol Motil* 17:274–278, 2011
66. Iyer PG, Borah BJ, Heien HC, Das A, Cooper GS, Chak A: Association of Barrett's esophagus with type II diabetes mellitus: results from a large population-based case-control study. *Clin Gastroenterol Hepatol* 11:1108–1114.e5, 2013
67. Pandolfino JE, El-Serag HB, Zhang Q, Shah N, Ghosh SK, Kahrilas PJ: Obesity: a challenge to esophagogastric junction integrity. *Gastroenterology* 130:639–649, 2006
68. Wu JC, Mui LM, Cheung CM, Chan Y, Sung JJ: Obesity is associated with increased transient lower esophageal sphincter relaxation. *Gastroenterology* 132:883–889, 2007
69. El-Serag HB, Ergun GA, Pandolfino J, Fitzgerald S, Tran T, Kramer JR: Obesity increases oesophageal acid exposure. *Gut* 56:749–755, 2007
70. Lagergren J, Mattsson F, Nyren O: Gastroesophageal reflux does not alter effects of body mass index on risk of esophageal adenocarcinoma. *Clin Gastroenterol Hepatol* 12:45–51, 2014
71. Schiller LR, Santa Ana CA, Schmulen AC, Hendler RS, Harford WV, Fordtran JS: Pathogenesis of fecal incontinence in diabetes mellitus: evidence for internal-anal-sphincter dysfunction. *N Engl J Med* 307:1666–1671, 1982
72. Wald A, Tunuguntla AK: Anorectal sensorimotor dysfunction in fecal incontinence and diabetes mellitus. Modification with biofeedback therapy. *N Engl J Med* 310:1282–1287, 1984
73. Rogers J, Levy DM, Henry MM, Misiewicz JJ: Pelvic floor neuropathy: a comparative study of diabetes mellitus and idiopathic faecal incontinence. *Gut* 29:756–761, 1988
74. Caruana BJ, Wald A, Hinds JP, Eidelman BH: Anorectal sensory and motor function in neurogenic fecal incontinence. Comparison between multiple sclerosis and diabetes mellitus. *Gastroenterology* 100:465–470, 1991
75. Russo A, Botten R, Kong MF, Chapman IM, Fraser RJ, Horowitz M, Sun WM: Effects of acute hyperglycaemia on anorectal motor and sensory function in diabetes mellitus. *Diabet Med* 21:176–182, 2004
76. Pazzi P, Scagliarini R, Gamberini S, Pezzoli A: Review article: gall-bladder motor function in diabetes mellitus. *Aliment Pharmacol Ther* 14(Suppl 2):62–65, 2000
77. Sanchez JC, Cabrera-Rode E, Sorell L, Galvan JA, Hernandez A, Molina G, Perich PA, Licea ME, Dominguez E, Diaz-Horta O: Celiac disease associated antibodies in persons with latent autoimmune diabetes of adult and type 2 diabetes. *Autoimmunity* 40:103–107, 2007
78. Kucera P, Novakova D, Behanova M, Novak J, Tlaskalova-Hogenova H, Andel M: Gliadin, endomysial and thyroid antibodies in patients with latent autoimmune diabetes of adults (LADA). *Clin Exp Immunol* 133:139–143, 2003
79. Romanos J, Rosen A, Kumar V, Trynka G, Franke L, Szperl A, Gutierrez-Achury J, van Diemen CC, Kanninga R, Jankipersadsing SA, Steck A, Eisenbarth G, van Heel DA, Cukrowska B, Bruno V, Mazzilli MC, Nunez C, Bilbao JR, Mearin ML, Barisani D, Rewers M, Norris JM, Ivarsson A, Boezen HM, Liu E, Wijmenga C; PreventCD Group: Improving coeliac disease risk prediction by testing non-HLA variants additional to HLA variants. *Gut* 63:415–422, 2014
80. du Pre MF, Sollid LM: T-cell and B-cell immunity in celiac disease. *Best Pract Res Clin Gastroenterol* 29:413–423, 2015
81. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA; American College of Gastroenterology: ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol* 108:656–676, 2013
82. Junker Y, Zeissig S, Kim SJ, Barisani D, Wieser H, Leffler DA, Zevallos V, Libermann TA, Dillon S, Freitag TL, Kelly CP, Schuppan D: Wheat amylase trypsin inhibitors drive intestinal inflammation via activation of toll-like receptor 4. *J Exp Med* 209:2395–2408, 2012
83. Abadie V, Sollid LM, Barreiro LB, Jabri B: Integration of genetic and immunological insights into a model of celiac disease pathogenesis. *Annu Rev Immunol* 29:493–525, 2011
84. Rewers M, Eisenbarth GS: Autoimmunity: celiac disease in T1DM—the need to look long term. *Nat Rev Endocrinol* 8:7–8, 2011
85. Ghawil M, Miotti V, Tonutti E, Tenore A, Hadeed I, Sindici C, Visentini D, Morgham A, Abusrewil S: HLA-DQ types of celiac disease in Libyan children with type 1 diabetes mellitus. *Eur J Gastroenterol Hepatol* 24:59–63, 2012
86. Walker MM, Murray JA: An update in the diagnosis of coeliac disease. *Histopathology* 59:166–179, 2011
87. Rubio-Tapia A, Murray JA: Celiac disease beyond the gut. *Clin Gastroenterol Hepatol* 6:722–723, 2008
88. Potter DD, Murray JA, Donohue JH, Burgart LJ, Nagorney DM, van Heerden JA, Plevak MF, Zinsmeister AR, Thibodeau SN: The role of defective mismatch repair in small bowel adenocarcinoma in celiac disease. *Cancer Res* 64:7073–7077, 2004
89. Rubio-Tapia A, Ludvigsson JF, Brantner TL, Murray JA, Everhart JE: The prevalence of celiac disease in the United States. *Am J Gastroenterol* 107:1538–1544, 2012
90. Rubio-Tapia A, Murray JA: Celiac disease. In *GI Epidemiology*. Talley NJ, Locke GR 3rd, Saito YA, Eds. Malden, Blackwell Publishing, 2007, p. 157–163
91. Fasano A, Berti I, Gerarduzzi T, Not T, Colletti RB, Drago S, Elitsur Y, Green PH, Guandalini S, Hill ID, Pietzak M, Ventura A, Thorpe M, Kryszak D, Fornaroli F, Wasserman SS, Murray JA, Horvath K: Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. *Arch Intern Med* 163:286–292, 2003
92. Rubio-Tapia A, Van Dyke CT, Lahr BD, Zinsmeister AR, El-Youssef M, Moore SB, Bowman M, Burgart LJ, Melton LJ 3rd, Murray JA: Predictors of family risk for celiac disease: a population-based study. *Clin Gastroenterol Hepatol* 6:983–987, 2008
93. Book L, Zone JJ, Neuhausen SL: Prevalence of celiac disease among relatives of sib pairs with celiac disease in U.S. families. *Am J Gastroenterol* 98:377–381, 2003

94. Mahmud FH, Murray JA, Kudva YC, Zinsmeister AR, Dierkhising RA, Lahr BD, Dyck PJ, Kyle RA, El-Youssef M, Burgart LJ, Van Dyke CT, Brogan DL, Melton LJ: Celiac disease in type 1 diabetes mellitus in a North American community: prevalence, serologic screening, and clinical features. *Mayo Clin Proc* 80:1429–1434, 2005
95. Dube C, Rostom A, Sy R, Cranney A, Saloojee N, Garritty C, Sampson M, Zhang L, Yazdi F, Mamaladze V, Pan I, Macneil J, Mack D, Patel D, Moher D: The prevalence of celiac disease in average-risk and at-risk Western European populations: a systematic review. *Gastroenterology* 128:S57–S67, 2005
96. Kaistha A, Castells S: Celiac disease in African American children with type 1 diabetes mellitus in inner city Brooklyn. *Pediatr Endocrinol Rev* 5(Suppl 4):994–998, 2008
97. Norris JM, Barriga K, Hoffenberg EJ, Taki I, Miao D, Haas JE, Emery LM, Sokol RJ, Erlich HA, Eisenbarth GS, Rewers M: Risk of celiac disease autoimmunity and timing of gluten introduction in the diet of infants at increased risk of disease. *JAMA* 293:2343–2351, 2005
98. Barera G, Bonfanti R, Viscardi M, Bazzigaluppi E, Calori G, Meschi F, Bianchi C, Chiumello G: Occurrence of celiac disease after onset of type 1 diabetes: a 6-year prospective longitudinal study. *Pediatrics* 109:833–838, 2002
99. Cerutti F, Bruno G, Chiarelli F, Lorini R, Meschi F, Sacchetti C; Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology: Younger age at onset and sex predict celiac disease in children and adolescents with type 1 diabetes: an Italian multicenter study. *Diabetes Care* 27:1294–1298, 2004
100. Ludvigsson JF, Ludvigsson J, Ekbom A, Montgomery SM: Celiac disease and risk of subsequent type 1 diabetes: a general population cohort study of children and adolescents. *Diabetes Care* 29:2483–2488, 2006
101. Lionetti E, Castellaneta S, Francavilla R, Pulvirenti A, Tonutti E, Amarri S, Barbato M, Barbera C, Barera G, Bellantoni A, Castellano E, Guariso G, Limongelli MG, Pellegrino S, Polloni C, Ughi C, Zuin G, Fasano A, Catassi C; SIGENP (Italian Society of Pediatric Gastroenterology, Hepatology, and Nutrition) Working Group on Weaning and CD Risk: Introduction of gluten, HLA status, and the risk of celiac disease in children. *N Engl J Med* 371:1295–1303, 2014
102. Vriezinga SL, Auricchio R, Bravi E, Castillejo G, Chmielewska A, Crespo Escobar P, Kolacek S, Koletzko S, Korponay-Szabo IR, Mummert E, Polanco I, Putter H, Ribes-Koninckx C, Shamir R, Szajewska H, Werkstetter K, Greco L, Gyimesi J, Hartman C, Hogen Esch C, Hopman E, Ivarsson A, Koltai T, Koning F, Martinez-Ojinaga E, te Marvelde C, Pavic A, Romanos J, Stoopman E, Villanacci V, Wijmenga C, Troncone R, Mearin ML: Randomized feeding intervention in infants at high risk for celiac disease. *N Engl J Med* 371:1304–1315, 2014
103. Evans KE, Aziz I, Cross SS, Sahota GR, Hopper AD, Hadjivassiliou M, Sanders DS: A prospective study of duodenal bulb biopsy in newly diagnosed and established adult celiac disease. *Am J Gastroenterol* 106:1837–1842, 2011
104. Waisbourd-Zinman O, Hojsak I, Rosenbach Y, Mozer-Glassberg Y, Shalitin S, Phillip M, Shamir R: Spontaneous normalization of anti-tissue transglutaminase antibody levels is common in children with type 1 diabetes mellitus. *Dig Dis Sci* 57:1314–1320, 2012
105. Simmons JH, Klingensmith GJ, McFann K, Rewers M, Ide LM, Taki I, Liu E, Hoffenberg EJ: Celiac autoimmunity in children with type 1 diabetes: a two-year follow-up. *J Pediatr* 158:276–281.e1, 2011
106. Husby S, Koletzko S, Korponay-Szabo IR, Mearin ML, Phillips A, Shamir R, Troncone R, Giersiepen K, Branski D, Catassi C, Lelgeman M, Maki M, Ribes-Koninckx C, Ventura A, Zimmer KP; ESPGHAN Working Group on Coeliac Disease Diagnosis; ESPGHAN Gastroenterology Committee; European Society for Pediatric Gastroenterology, Hepatology, and Nutrition: European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr* 54:136–160, 2012
107. Rubio-Tapia A, Kyle RA, Kaplan EL, Johnson DR, Page W, Erdtmann F, Brantner TL, Kim WR, Phelps TK, Lahr BD, Zinsmeister AR, Melton LJ 3rd, Murray JA: Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology* 137:88–93, 2009
108. Kurppa K, Collin P, Maki M, Kaukinen K: Celiac disease and health-related quality of life. *Expert Rev Gastroenterol Hepatol* 5:83–90, 2011
109. Camarca ME, Mozzillo E, Nugnes R, Zito E, Falco M, Fattorusso V, Mobilia S, Buono P, Valerio G, Troncone R, Franzese A: Celiac disease in type 1 diabetes mellitus. *Ital J Pediatr* 38:10, 2012
110. Sud S, Marcon M, Assor E, Daneman D, Mahmud FH: Quality of life in children with diabetes and celiac disease: minimal impact of the 'double diagnosis'. *Pediatr Diabetes* 13:163–169, 2012
111. Paavola A, Kurppa K, Ukkola A, Collin P, Lahdeaho ML, Huhtala H, Maki M, Kaukinen K: Gastrointestinal symptoms and quality of life in screen-detected celiac disease. *Dig Liver Dis* 44:814–818, 2012
112. Artz E, Warren-Ulanch J, Becker D, Greenspan S, Freemark M: Seropositivity to celiac antigens in asymptomatic children with type 1 diabetes mellitus: association with weight, height, and bone mineralization. *Pediatr Diabetes* 9:277–284, 2008
113. Leeds JS, Hopper AD, Hadjivassiliou M, Tesfaye S, Sanders DS: High prevalence of microvascular complications in adults with type 1 diabetes and newly diagnosed celiac disease. *Diabetes Care* 34:2158–2163, 2011
114. Mollazadegan K, Kugelberg M, Montgomery SM, Sanders DS, Ludvigsson J, Ludvigsson JF: A population-based study of the risk of diabetic retinopathy in patients with type 1 diabetes and celiac disease. *Diabetes Care* 36:316–321, 2013
115. Malalasekera V, Cameron F, Grixti E, Thomas MC: Potential reno-protective effects of a gluten-free diet in type 1 diabetes. *Diabetologia* 52:798–800, 2009
116. Skovbjerg H, Tarnow L, Locht H, Parving HH: The prevalence of coeliac disease in adult Danish patients with type 1 diabetes with and without nephropathy. *Diabetologia* 48:1416–1417, 2005
117. Picarelli A, Sabbatella L, Di Tola M, Vetrano S, Casale C, Anania MC, Porowska B, Vergari M, Schiaffini R, Gargiulo P: Anti-endomysial antibody of IgG1 isotype detection strongly increases the prevalence of coeliac disease in patients affected by type I diabetes mellitus. *Clin Exp Immunol* 142:111–115, 2005
118. Hummel S, Pfluger M, Hummel M, Bonifacio E, Ziegler AG: Primary dietary intervention study to reduce the risk of islet autoimmunity in children at increased risk for type 1 diabetes: the BABYDIET study. *Diabetes Care* 34:1301–1305, 2011
119. Norris JM, Barriga K, Klingensmith G, Hoffman M, Eisenbarth GS, Erlich HA, Rewers M: Timing of initial cereal exposure in infancy and risk of islet autoimmunity. *JAMA* 290:1713–1720, 2003

120. Wang K, Baldassano R, Zhang H, Qu HQ, Imielinski M, Kugathasan S, Annese V, Dubinsky M, Rotter JI, Russell RK, Bradfield JP, Sleiman PM, Glessner JT, Walters T, Hou C, Kim C, Frackelton EC, Garris M, Doran J, Romano C, Catassi C, Van Limbergen J, Guthery SL, Denson L, Piccoli D, Silverberg MS, Stanley CA, Monos D, Wilson DC, Griffiths A, Grant SF, Satsangi J, Polychronakos C, Hakonarson H: Comparative genetic analysis of inflammatory bowel disease and type 1 diabetes implicates multiple loci with opposite effects. *Hum Mol Genet* 19:2059–2067, 2010
121. Kappelman MD, Galanko JA, Porter CQ, Sandler RS: Association of paediatric inflammatory bowel disease with other immune-mediated diseases. *Arch Dis Child* 96:1042–1046, 2011
122. Cohen R, Robinson D, Jr., Paramore C, Fraeman K, Renahan K, Bala M: Autoimmune disease concomitance among inflammatory bowel disease patients in the United States, 2001–2002. *Inflamm Bowel Dis* 14:738–743, 2008
123. Hemminki K, Li X, Sundquist J, Sundquist K: Familial association between type 1 diabetes and other autoimmune and related diseases. *Diabetologia* 52:1820–1828, 2009
124. Akerkar GA, Peppercorn MA, Hamel MB, Parker RA: Corticosteroid-associated complications in elderly Crohn's disease patients. *Am J Gastroenterol* 92:461–464, 1997
125. Ungar B, Stocks AE, Martin FI, Whittingham S, Mackay IR: Intrinsic-factor antibody, parietal-cell antibody, and latent pernicious anaemia in diabetes mellitus. *Lancet* 2:415–417, 1968
126. De Block CE, De Leeuw IH, Bogers JJ, Pelckmans PA, Ieven MM, Van Marck EA, Van Hoof V, Maday E, Van Acker KL, Van Gaal LF: Helicobacter pylori, parietal cell antibodies and autoimmune gastropathy in type 1 diabetes mellitus. *Aliment Pharmacol Ther* 16:281–289, 2002
127. Alonso N, Granada ML, Soldevila B, Salinas I, Joaquin C, Reverter JL, Junca J, Martinez Caceres EM, Sanmarti A: Serum autoimmune gastritis markers, pepsinogen I and parietal cell antibodies, in patients with type 1 diabetes mellitus: a 5-year prospective study. *J Endocrinol Invest* 34:340–344, 2011
128. Borch K, Renvall H, Liedberg G: Gastric endocrine cell hyperplasia and carcinoid tumors in pernicious anemia. *Gastroenterology* 88:638–648, 1985
129. Wenzlau JM, Gardner TJ, Frisch LM, Davidson HW, Hutton JC: Development of a novel autoantibody assay for autoimmune gastritis in type 1 diabetic individuals. *Diabetes Metab Res Rev* 27:887–890, 2011
130. Maclaren NK, Riley WJ: Thyroid, gastric, and adrenal autoimmunities associated with insulin-dependent diabetes mellitus. *Diabetes Care* 8(Suppl 1):34–38, 1985
131. Drossman DA: The functional gastrointestinal disorders and the Rome III process. *Gastroenterology* 130:1377–1390, 2006
132. Manning AP, Thompson WG, Heaton KW, Morris AF: Towards positive diagnosis of the irritable bowel. *Br Med J* 2:653–654, 1978
133. Dubois PC, Trynka G, Franke L, Hunt KA, Romanos J, Curtotti A, Zhernakova A, Heap GA, Adany R, Aromaa A, Bardella MT, van den Berg LH, Bockett NA, de la Concha EG, Dema B, Fehrmann RS, Fernandez-Arquero M, Fiatal S, Grandone E, Green PM, Groen HJ, Gwilliam R, Houwen RH, Hunt SE, Kaukinen K, Kelleher D, Korponay-Szabo I, Kurppa K, MacMathuna P, Maki M, Mazzilli MC, McCann OT, Mearin ML, Mein CA, Mirza MM, Mistry V, Mora B, Morley KI, Mulder CJ, Murray JA, Nunez C, Oosterom E, Ophoff RA, Polanco I, Peltonen L, Platteel M, Rybak A, Salomaa V, Schweizer JJ, Sperandeo MP, Tack GJ, Turner G, Veldink JH, Verbeek WH, Weersma RK, Wolters VM, Urcelay E, Cukrowska B, Greco L, Neuhausen SL, McManus R, Barisani D, Deloukas P, Barrett JC, Saavalainen P, Wijmenga C, van Heel DA: Multiple common variants for celiac disease influencing immune gene expression. *Nat Genet* 42:295–302, 2010
134. Smyth DJ, Plagnol V, Walker NM, Cooper JD, Downes K, Yang JH, Howson JM, Stevens H, McManus R, Wijmenga C, Heap GA, Dubois PC, Clayton DG, Hunt KA, van Heel DA, Todd JA: Shared and distinct genetic variants in type 1 diabetes and celiac disease. *N Engl J Med* 359:2767–2777, 2008
135. Eyre S, Hinks A, Bowes J, Flynn E, Martin P, Wilson AG, Morgan AW, Emery P, Steer S, Hocking LJ, Reid DM, Harrison P, Wordsworth P, Thomson W, Worthington J, Barton A; Yorkshire Early Arthritis Consortium; Biologics in RA Control Consortium: Overlapping genetic susceptibility variants between three autoimmune disorders: rheumatoid arthritis, type 1 diabetes and coeliac disease. *Arthritis Res Ther* 12:R175, 2010
136. Rossi TM, Albini CH, Kumar V: Incidence of celiac disease identified by the presence of serum endomysial antibodies in children with chronic diarrhea, short stature, or insulin-dependent diabetes mellitus. *J Pediatr* 123:262–264, 1993
137. Talal AH, Murray JA, Goeken JA, Sivitz WI: Celiac disease in an adult population with insulin-dependent diabetes mellitus: use of endomysial antibody testing. *Am J Gastroenterol* 92:1280–1284, 1997
138. Aktay AN, Lee PC, Kumar V, Parton E, Wyatt DT, Werlin SL: The prevalence and clinical characteristics of celiac disease in juvenile diabetes in Wisconsin. *J Pediatr Gastroenterol Nutr* 33:462–465, 2001
139. Rewers M, Liu E, Simmons J, Redondo MJ, Hoffenberg EJ: Celiac disease associated with type 1 diabetes mellitus. *Endocrinol Metab Clin North Am* 33:197–214, 2004
140. Fraser-Reynolds KA, Butzner JD, Stephure DK, Trussell RA, Scott RB: Use of immunoglobulin A-antiendomysial antibody to screen for celiac disease in North American children with type 1 diabetes. *Diabetes Care* 21:1985–1989, 1998
141. Gillett PM, Gillett HR, Israel DM, Metzger DL, Stewart L, Chanoine JP, Freeman HJ: High prevalence of celiac disease in patients with type 1 diabetes detected by antibodies to endomysium and tissue transglutaminase. *Can J Gastroenterol* 15:297–301, 2001
142. Remes-Troche JM, Rios-Vaca A, Ramirez-Iglesias MT, Rubio-Tapia A, Andrade-Zarate V, Rodriguez-Vallejo F, Lopez-Maldonado F, Gomez-Perez FJ, Uscanga LF: High prevalence of celiac disease in Mexican Mestizo adults with type 1 diabetes mellitus. *J Clin Gastroenterol* 42:460–465, 2008
143. Koletzko S, Burgin-Wolff A, Koletzko B, Knapp M, Burger W, Gruneklee D, Herz G, Ruch W, Thon A, Wendel U, Zuppinger K: Prevalence of coeliac disease in diabetic children and adolescents. A multicentre study. *Eur J Pediatr* 148:113–117, 1988
144. Carlsson AK, Axelsson IE, Borulf SK, Bredberg AC, Lindberg BA, Sjoberg KG, Ivarsson SA: Prevalence of IgA-antiendomysium and IgA-antigliadin autoantibodies at diagnosis of insulin-dependent diabetes mellitus in Swedish children and adolescents. *Pediatrics* 103:1248–1252, 1999
145. Narula P, Porter L, Langton J, Rao V, Davies P, Cummins C, Kirk J, Barrett T, Protheroe S: Gastrointestinal symptoms in children with type 1 diabetes screened for celiac disease. *Pediatrics* 124:E489–E495, 2009

146. Bhadada SK, Kochhar R, Bhansali A, Dutta U, Kumar PR, Poornachandra KS, Vaiphei K, Nain CK, Singh K: Prevalence and clinical profile of celiac disease in type 1 diabetes mellitus in north India. *J Gastroenterol Hepatol* 26:378–381, 2011
147. Hummel M, Bonifacio E, Stern M, Dittler J, Schimmel A, Ziegler AG: Development of celiac disease-associated antibodies in offspring of parents with type I diabetes. *Diabetologia* 43:1005–1011, 2000
148. Jaeger C, Hatziagelaki E, Petzoldt R, Bretzel RG: Comparative analysis of organ-specific autoantibodies and celiac disease-associated antibodies in type 1 diabetic patients, their first-degree relatives, and healthy control subjects. *Diabetes Care* 24:27–32, 2001
149. Hummel S, Hummel M, Banholzer J, Hanak D, Mollenhauer U, Bonifacio E, Ziegler AG: Development of autoimmunity to transglutaminase C in children of patients with type 1 diabetes: relationship to islet autoantibodies and infant feeding. *Diabetologia* 50:390–394, 2007
150. Saukkonen T, Vaisanen S, Akerblom HK, Savilahti E; Childhood Diabetes in Finland Study Group: Coeliac disease in children and adolescents with type 1 diabetes: a study of growth, glycaemic control, and experiences of families. *Acta Paediatr* 91:297–302, 2002
151. Sanchez-Albisua I, Wolf J, Neu A, Geiger H, Wascher I, Stern M: Coeliac disease in children with type 1 diabetes mellitus: the effect of the gluten-free diet. *Diabet Med* 22:1079–1082, 2005
152. Hansen D, Brock-Jacobsen B, Lund E, Bjorn C, Hansen LP, Nielsen C, Fenger C, Lillevang ST, Husby S: Clinical benefit of a gluten-free diet in type 1 diabetic children with screening-detected celiac disease: a population-based screening study with 2 years' follow-up. *Diabetes Care* 29:2452–2456, 2006
153. Taler I, Phillip M, Lebenthal Y, de Vries L, Shamir R, Shalitin S: Growth and metabolic control in patients with type 1 diabetes and celiac disease: a longitudinal observational case-control study. *Pediatr Diabetes* 13:597–606, 2012
154. Acerini CL, Ahmed ML, Ross KM, Sullivan PB, Bird G, Dunger DB: Coeliac disease in children and adolescents with IDDM: clinical characteristics and response to gluten-free diet. *Diabet Med* 15:38–44, 1998
155. Westman E, Ambler GR, Royle M, Peat J, Chan A: Children with coeliac disease and insulin dependent diabetes mellitus—growth, diabetes control and dietary intake. *J Pediatr Endocrinol Metab* 12:433–442, 1999
156. Valerio G, Spadaro R, Iafusco D, Lombardi F, Del Puente A, Esposito A, De Terlizzi F, Prisco F, Troncone R, Franzese A: The influence of gluten free diet on quantitative ultrasound of proximal phalanxes in children and adolescents with type 1 diabetes mellitus and celiac disease. *Bone* 43:322–326, 2008
157. Saadah OI, Zacharin M, O'Callaghan A, Oliver MR, Catto-Smith AG: Effect of gluten-free diet and adherence on growth and diabetic control in diabetics with coeliac disease. *Arch Dis Child* 89:871–876, 2004
158. Simmons JH, Klingensmith GJ, McFann K, Rewers M, Taylor J, Emery LM, Taki I, Vanyi S, Liu E, Hoffenberg EJ: Impact of celiac autoimmunity on children with type 1 diabetes. *J Pediatr* 150:461–466, 2007
159. Rami B, Sumnik Z, Schober E, Waldhor T, Battelino T, Bratanic N, Kurti K, Lebl J, Limbert C, Madacsy L, Odink RJ, Paskova M, Soltesz G: Screening detected celiac disease in children with type 1 diabetes mellitus: effect on the clinical course (a case control study). *J Pediatr Gastroenterol Nutr* 41:317–321, 2005
160. Amin R, Murphy N, Edge J, Ahmed ML, Acerini CL, Dunger DB: A longitudinal study of the effects of a gluten-free diet on glycemic control and weight gain in subjects with type 1 diabetes and celiac disease. *Diabetes Care* 25:1117–1122, 2002
161. Kaspers S, Kordonouri O, Schober E, Grabert M, Hauffa BP, Holl RW; German Working Group for Pediatric Diabetology: Anthropometry, metabolic control, and thyroid autoimmunity in type 1 diabetes with celiac disease: a multicenter survey. *J Pediatr* 145:790–795, 2004
162. Frohlich-Reiterer EE, Kaspers S, Hofer S, Schober E, Kordonouri O, Pozza SB, Holl RW; Diabetes Patienten Verlaufsdokumentationssystem-Wiss Study Group: Anthropometry, metabolic control, and follow-up in children and adolescents with type 1 diabetes mellitus and biopsy-proven celiac disease. *J Pediatr* 158:589–593.e2, 2011
163. Pham-Short A, Donaghue KC, Ambler G, Chan AK, Hing S, Cusumano J, Craig ME: Early elevation of albumin excretion rate is associated with poor gluten-free diet adherence in young people with coeliac disease and diabetes. *Diabet Med* 31:208–212, 2014
164. Riley WJ, Toskes PP, Maclaren NK, Silverstein JH: Predictive value of gastric parietal cell autoantibodies as a marker for gastric and hematologic abnormalities associated with insulin-dependent diabetes. *Diabetes* 31:1051–1055, 1982
165. Goldstein DE, Drash A, Gibbs J, Blizzard RM: Diabetes mellitus: the incidence of circulating antibodies against thyroid, gastric, and adrenal tissue. *J Pediatr* 77:304–306, 1970
166. Kokkonen J: Parietal cell antibodies and gastric secretion in children with diabetes mellitus. *Acta Paediatr Scand* 69:485–489, 1980
167. Irvine WJ, Clarke BF, Scarth L, Cullen DR, Duncan LJ: Thyroid and gastric autoimmunity in patients with diabetes mellitus. *Lancet* 2:163–168, 1970