among patients with type 1 diabetes, but the reason for this is unclear.[7,8] It may be due to a genetic polymorphism in the gene encoding β-defensin 1.[8] However, there is no evidence that this genetic difference leads to an immunocompromised state allowing invasive fungal disease to occur. There have been case reports of patients with type 1 diabetes and diabetic ketoacidosis in whom severe opportunistic infections have developed.[9] The increased susceptibility may be attributed to the short-term acidic environment of diabetic ketoacidosis, which is ideal for certain opportunistic pathogens.

In summary, there is insufficient evidence to conclude that children with type 1 diabetes mellitus are immunocompromised. The evidence indicates that an immunocompromised state occurs only in the context of poor glycemic control with severe complications such as diabetic ketoacidosis or in adults with vasculopathy and peripheral neuropathy. Fortunately, with modern standards of care and education of families to manage intercurrent illness in their children with type 1 diabetes mellitus, hospital admission for diabetic ketoacidosis is now rare.

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References

1. Mater A, Al-Sulaiti G, Johnston DL, Slinger R. A 4-year-old child with leukemia and an enlarging arm lesion. *CMAJ* 2005;172(3):332.
2. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis:a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect* 2004;10(Suppl 1):31-47.
3. Boyd AS, Wiser B, Sams HH, King LE. Gangrenous cutaneous mucormycosis in a child with a solid organ transplant: a case report and review of the literature. *Pediatr Dermatol* 2003;20:411-5.
4. Calvet H, Yoshikawa TT. Infections in diabetes. *Infect Dis Clin North Am* 2001;15:407-21.
5. Moutschen MP, Scheen AJ, Lefebvre PJ. Impaired immune responses in diabetes mellitus: analysis of the factors and mechanisms involved. Relevance to the increased susceptibility of diabetic patients to specific infections. *Diabete Metab* 1992;18:187-201.
6. Diepersloot RJA, Bouter KP, Beyer WEP, Hoekstra JBL, Masurel N. Humoral immune response and delayed type hypersensitivity to influenza vaccine in patients with diabetes mellitus. *Diabetologia* 1987;30:397-401.
7. Willis AM, Coulter WA, Fulton CR, Hayes JR, Bell PM, Lamey PJ. Oral candidal carriage and infection in insulin-treated diabetic patients. *Diabet Med* 1999;16:675-9.
8. Jurevic RJ, Bai M, Chadwick RB, White TC, Dale BA. Single-nucleotide polymorphisms (SNPs) in human β-defensin 1: high-throughput SNP assays and association with *Candida* carriage in type I diabetics and nondiabetic controls. *J Clin Microbiol* 2003;41:90-6.
9. Moye J, Rosenbloom AL, Silverstein J. Clinical predictors of mucormycosis in children with type 1 diabetes mellitus. *J Pediatr Endocrinol Metab* 2002;15:1001-4.

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Effect of thiazolidinediones on lipid profile

In their review of oral hypoglycemic therapy in type 2 diabetes mellitus, Alice Cheng and George Fantus[1] mention the effect of thiazolidinediones on high-density lipoprotein (HDL) cholesterol; I would like to add some comments about the effects of these agents on low-density lipoprotein (LDL) cholesterol and triglycerides.

In fact, the effect of thiazolidinediones on serum lipids and lipoproteins varies with the agent used (pioglitazone or rosiglitazone). As noted by Cheng and Fantus, HDL levels increase with either of these 2 drugs.[2–7] However, LDL cholesterol levels remain unchanged with pioglitazone monotherapy or a combination of pioglitazone with other oral hypoglycemic agents or insulin.[2–4] In contrast, LDL cholesterol levels increase with rosiglitazone monotherapy or combination therapy.[5–7] Although pioglitazone has been associated with a decrease in triglyceride levels,[2–4] the effects of rosiglitazone on triglycerides have been variable, ranging from a 2% increase to a 19% decrease.[6,7]

Studies directly comparing the 2 agents are scant, and the cause of this variation in lipid levels is unknown.

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References

1. Cheng AYY, Fantus IG. Oral antihyperglycemic therapy for type 2 diabetes mellitus. *CMAJ* 2005;172(2):213-26.
2. Rosenblatt S, Miskin B, Glazer NB, Prince MJ, Robertson KE; Pioglitazone 026 Study Group. The impact of pioglitazone on glycemic control and atherogenic dyslipidemia in patients with type 2 diabetes mellitus. *Coron Artery Dis* 2001; 12:413-23.
3. Kipnes MS, Krosnick A, Rendell MS, Egan JW, Mathisen AL, Schneider RL. Pioglitazone hydrochloride in combination with sulfonylurea therapy improves glycemic control in patients with type 2 diabetes mellitus: a randomized, placebo-controlled study. *Am J Med* 2001; 111:10-7.
4. Rosenstock J, Einhorn D, Hershon K, Glazer NB, Yu S. Efficacy and safety of pioglitazone in type 2 diabetes: a randomised, placebo-controlled study in patients receiving stable insulin therapy. *Int J Clin Pract* 2002;56:251-7.
5. Lebovitz HE, Dole JF, Patwardhan R, Rappaport EB, Freed MI; Rosiglitazone Clinical Trials Study Group. Rosiglitazone monotherapy is effective in patients with type 2 diabetes [published errata appear in *J Clin Endocrinol Metab* 2001;86:1659, 2002;87:iv]. *J Clin Endocrinol Metab* 2001;86:280-8.
6. Fonseca V, Rosenstock J, Patwardhan R, Salzman A. Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus: a randomized controlled trial [published erratum appears in *JAMA* 2000;284: 1384]. *JAMA* 2000;283:1695-702.
7. Raskin P, Rendell M, Riddle MC, Dole JF, Freed MI, Rosenstock J. A randomized trial of rosiglitazone therapy in patients with inadequately controlled insulin-treated type 2 diabetes. *Diabetes Care* 2001;24:1226-32.

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[The authors respond:]

We appreciate Pankaj Madan's supplementary information to our article on oral antihyperglycemic therapy.[1] As Madan has correctly outlined, the studies comparing pioglitazone (monotherapy or combination therapy) with placebo have demonstrated no changes in LDL cholesterol,[2–4] whereas studies comparing rosiglitazone (monotherapy or combination therapy) with placebo have demonstrated an increase, ranging from 8% to 19%, in LDL cholesterol.[5–7] In clinical practice, this elevation may have a small impact, if any, for patients with diabetes mellitus using lipid-lowering therapy (statins) to achieve target LDL levels.[8,9]

The lack of direct-comparison studies makes it difficult to draw definitive conclusions regarding the lipid differences between the 2 medications. Simi-

larly, significantly elevated triglyceride levels might best be targeted directly with fibrates.

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References

1. Cheng AYY, Fantus IG. Oral antihyperglycemic therapy for type 2 diabetes mellitus. *CMAJ* 2005;172(2):213-26.
2. Rosenblatt S, Miskin B, Glazer NB, Prince MJ, Robertson KE; Pioglitazone 026 Study Group. The impact of pioglitazone on glycemic control and atherogenic dyslipidemia in patients with type 2 diabetes mellitus. *Coron Artery Dis* 2001; 12:413-23.
3. Kipnes MS, Krosnick A, Rendell MS, Egan JW, Mathisen AL, Schneider RL. Pioglitazone hydrochloride in combination with sulfonylurea therapy improves glycemic control in patients with type 2 diabetes mellitus: a randomized, placebo-controlled study. *Am J Med* 2001; 111:10-7.
4. Rosenstock J, Einhorn D, Hershon K, Glazer NB, Yu S. Efficacy and safety of pioglitazone in type 2 diabetes: a randomised, placebo-controlled study in patients receiving stable insulin therapy. *Int J Clin Pract* 2002;56:251-7.
5. Lebovitz HE, Dole JF, Patwardhan R, Rappaport EB, Freed MI; Rosiglitazone Clinical Trials Study Group. Rosiglitazone monotherapy is effective in patients with type 2 diabetes [published errata appear in *J Clin Endocrinol Metab* 2001;86:1659, 2002;87:iv]. *J Clin Endocrinol Metab* 2001;86:280-8.
6. Fonseca V, Rosenstock J, Patwardhan R, Salzman A. Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus: a randomized controlled trial [published erratum appears in *JAMA* 2000;284: 1384]. *JAMA* 2000;283:1695-702.
7. Raskin P, Rendell M, Riddle MC, Dole JF, Freed MI, Rosenstock J. A randomized trial of rosiglitazone therapy in patients with inadequately controlled insulin-treated type 2 diabetes. *Diabetes Care* 2001;24:1226-32.
8. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.
9. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004;364:685-96.

Competing interests: Dr. Fantus has received an honorarium for a lecture from Bristol Myers Squibb (distributor of metformin in the United States). None declared for Dr. Cheng.

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Benzene rings

A recent Clinical Vistas article[1] provides an interesting look at the similarity between homogentisic acid, which is excreted in the urine of people with alkaptonuria, and hydroquinone, which is used in the process to develop photographs. Unfortunately, both of the chemical structures provided in the article are wrong. Homogentisic acid and hydroquinone are both aromatic compounds (the author alludes to this by referring to the benzene ring of hydroquinone) that have a 6-membered, not an 8-membered, ring.

Perhaps a minor point, but worth correcting, because in chemistry, biochemistry and the medical arts and sciences, structure is everything.

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Reference

1. Maxwell D. Alkaptonuria and photography: a patient's urine tells the story. *CMAJ* 2005;172 (8):1002-3.

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[The author responds:]

I am most grateful to Dr. Atkinson for pointing out my error. He is, of course, absolutely correct. The error crept in when I tried to replicate my hand-drawn diagram, using a word-processing program to draw the chemical structure. As noted,[1] the chemical structures of homogentisic acid and hydroquinone are strikingly similar.

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Reference

1. Maxwell D. Alkaptonuria and photography: a patient's urine tells the story. *CMAJ* 2005;172 (8):1002-3.

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Corrections

In a recent article,[1] a link to an online version of Table 1 incorrectly lists the volume number as 1723 as opposed to 173.

Reference

1. Dendukuri N, Costa V, McGregor M, Brophy JM. Probiotic therapy for the prevention and treatment of *Clostridium difficile*-associated diarrhea: a systematic review. *CMAJ* 2005;173(2): 167-70.

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In a recent article,[1] the affiliations of 3 authors were mistakenly omitted. Patricia Pugh is the study coordinator (Newmarket, Ont.), Beverley Chalmers is an international health consultant (Kingston, Ont.) and Freda Seddon is a community midwife (Bobcaygeon, Ont.). We apologize for this error.

Reference

1. Carroll JC, Reid AJ, Biringer A, Midmer D, Glazier RH, Wilson L, et al. Effectiveness of the Antenatal Psychosocial Health Assessment (APHA) form in detecting psychosocial concerns: a randomized controlled trial. *CMAJ* 2005;173(3): 253-9.

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