trials is the reduction of potential bias, cointervention and contamination between treatment and control groups. All these factors will also influence the cost of patient satisfaction surveys.

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Niacin versus niacinamide

Dr. Anthony A.J. Walter's letter "Megavitamin and megamineral therapy in childhood" (*Can Med Assoc J* 1992; 146: 2140) indicates that perhaps niacinamide reduces serum cholesterol levels. This is not so: it seems that when the niacin molecule takes on an amide group the cholesterol-lowering as well as the vasodilating effects are inhibited.

This is a pity, since niacinamide could otherwise be widely used as a lipid-lowering agent. Patients have to be well motivated to comply with a niacin regimen. When they do so I have found niacin therapy to be very successful in the management of hypercholesterolemia.

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Dr. Walter raises several questions about the use of niacinamide as a substitute for niacin to reduce cholesterol levels. We wish to respond and to put into perspective the statements that he takes from our publication *Compendium of Pharmaceuticals and Specialties* (*CPS*).[1]

Niacinamide is not effective in lowering serum cholesterol levels and is therefore not approved for this purpose in Canada. Niacin and niacinamide are identical in their functions as vitamins, but their pharmacologic and toxic properties differ markedly with respect to other actions, including the lowering of cholesterol levels. The lipid-lowering effect of niacin has no relation to this agent's role as a vitamin.[2]

In high doses (more than 1 g) a lot of niacin remains unchanged; the serum concentrations of both low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) are reduced and that of high-density lipoprotein is increased.[3] The reduction of the VLDL level is rapid, and the magnitude of the decrease is dependent on the initial VLDL concentration. The LDL level decreases more slowly, with a maximum decrease after 3 to 5 weeks, the magnitude of which is related to the dose of niacin.[2]

The adverse effects of high doses of niacin are well documented: cutaneous flushing (especially of the face and neck) and pruritus occur within 20 minutes after administration and persist for 30 to 60 minutes. Tolerance usually develops after several weeks of therapy. Gastrointestinal upset is also common. Niacin may be given with food and divided into two to four doses daily. As Dr. Leonard I. Levine mentions (*ibid*: 104), increasing the dose gradually has been effective. Others have suggested the administration of acetylsalicylic acid, 325 mg, 30 minutes before the niacin to decrease the cutaneous vasodilation, which is thought to be mediated by prostaglandins.[2-4]

The *CPS* contains two separate monographs for niacin and niacinamide. These are general monographs, compiled by the *CPS* Drug Information Division and reviewed by the Editorial Advisory Panel. In the "Indications" section of the monographs it can be seen that niacin is indicated for the lowering of elevated serum cholesterol levels, whereas niacinamide is not. Niacin is converted to niacinamide in vivo, and this is necessary for its action as a vitamin. Niacinamide does not possess the cutaneous vasodilating properties of niacin and is therefore suitable as an alternative for the prevention of niacin deficiency or in the treatment of pellagra, for which it is indicated.[2,3]

We appreciate Walter's comments and will ensure that there is no potential for misinterpretation in the next edition of the *CPS*.

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