

## The cardiovascular health of the nation – should we be advocating a low-carbohydrate high-fat diet?

A spate of articles in the lay press have advocated a low-carbohydrate high-fat diet for cardiovascular health, questioning 'What's cholesterol got to do with it?' and whether cholesterol-lowering drugs, particularly statins, are doing more harm than good.

It is correct that excessive carbohydrate intake, particularly refined carbohydrates found in sugary drinks and energy snacks, is behind the global 'diabesity' epidemic of overweight, obesity and type 2 diabetes mellitus (T2DM). However, it is wrong to conclude that high carbohydrate intake is the major cause of atherosclerosis, the leading cause of cardiovascular disease (CVD). If a high-carbohydrate diet increases the risk for obesity and T2DM, and if diabetes is a risk factor for atherosclerosis, one cannot conclude that a high-carbohydrate diet is the cause of atherosclerosis.

Atherosclerosis, particularly coronary artery disease (CAD), is not a disease of carbohydrate metabolism and there is no evidence to support the measurement of carbohydrate or insulin resistance to identify atherosclerosis risk.<sup>1</sup> There is also little evidence that low-carbohydrate diets prevent atherosclerosis. Marathon runners who 'carbo-load' – consume large quantities of refined and complex carbohydrates before major events – are exquisitely sensitive to insulin, as they have a low percentage body fat and are in top physical condition.

If insulin resistance was the cause of atherosclerosis, patients with familial hypercholesterolaemia (FH) – who, if untreated, develop severe atherosclerosis and often die prematurely from CVD (particularly CAD) in their 40s or 50s – would have marked insulin resistance, which they do not.<sup>2</sup> In addition, small dense low-density lipoprotein cholesterol (LDL-C) particles, typical of the metabolic syndrome or T2DM, are thought to be more atherogenic. However, subjects with FH tend to have large LDL-C particles and are at much greater risk for atherosclerosis.<sup>3</sup>

Although there are several major risk factors for atherosclerosis, such as hypertension, diabetes and cigarette smoking, elevated LDL-C is the driving force. Hunter-gatherer populations still following an indigenous lifestyle show little or no evidence of atherosclerosis, even in individuals living into their 70s or 80s.<sup>4</sup> In populations of low serum cholesterol levels, such as the rural Chinese, CAD prevalence is also low, even in the presence of other CAD risk factors. Persons with genetically lifelong low LDL-C levels – resulting from hypobetalipoproteinaemia or loss-of-function mutations in the proprotein convertase subtilisin/kexin type 9 (PCSK9) gene – have a markedly reduced risk (80 - 90%) of developing CAD, despite a similar prevalence of other CVD risk factors.<sup>5</sup>

Innumerable epidemiological studies over more than 2 decades have shown overwhelming evidence that the more LDL-C is lowered, the lower the CAD risk. In fact, this is one of the most thoroughly researched and established facts of medicine.<sup>6</sup> For every 1 mmol/l reduction in LDL-C using statins (the most powerful drugs we currently have for lowering LDL-C) there is a 12% reduction in total mortality and a 21% reduction in major vascular events.<sup>7</sup> A threshold below which LDL-C reduction is no longer beneficial but harmful has not been identified,<sup>8</sup> we are born with 1 mmol/l LDL-C and it is probably only below this level that cholesterol synthesis becomes limiting.<sup>9</sup>

Established vascular disease and high-risk patients should not be denied the remarkable benefit of statin therapy. Rather than questioning the lipid hypothesis, we should be treating those in need earlier and more aggressively.<sup>10</sup> In FH patients it is essential to lower the LDL-C level with drug therapy, particularly statins, as diet is ineffective. Having treated patients with homo- and heterozygous FH

for over 20 years and seen the remarkable benefits of statin therapy, I have a low threshold to treat patients with these notably safe drugs.<sup>11</sup> This therapy has even prolonged life by 30+ years in subjects with homozygous FH.<sup>12</sup>

I also question whether diabetes is 'caused' by statin therapy.<sup>13</sup> I have not seen an increase in diabetes prevalence in FH patients despite treating them with high-dose statin therapy for over 20 years. Patients may be less compliant with diet adherence while 'on medication for cholesterol'; an increase in calorie intake may make them more susceptible to weight gain, obesity and ultimately to T2DM.

I urge us not to 'throw out the baby with the bathwater'. CVD is, and probably will remain, the leading cause of death worldwide for several decades. LDL-C is the pivotal CVD risk factor and needs to be addressed. Combined with a sedentary lifestyle, excess calorie intake, whether in the form of protein, carbohydrate or fat, is the major cause of the 'diabesity' epidemic contributing to, but not causing, atherosclerosis. Restriction of refined carbohydrates will assist with weight reduction in the short term. However, it is not correct, but rather potentially harmful, to advocate the substitution of refined carbohydrates with fats – particularly saturated fats.

We must encourage and promote a healthy lifestyle with regular exercise, and a healthy diet with moderate portions of all three major dietary components – carbohydrate, protein and fat.<sup>14</sup> Everything in moderation is the name of the game.

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