are initiated during or after the first trimester. For example, the odds ratio (OR) of risk of cardiovascular malformations attributable to administration of angiotensin-converting enzyme inhibitors during the first trimester amounts to 1.9 [95% confidence interval (CI) 0.5–7.2] and the corresponding OR attributable to other hypertensive classes (including β-adrenergic blockers, calcium channel blockers and diuretics) amounts to 1.7 (95% CI 1.1–2.8) during that period. The OR of the risk of pulmonary valve stenosis for anti-hypertensive drugs initiated during the first trimester amounts to 2.6 (95% CI 1.3–5.4), the corresponding OR for Ebstein malformation being 11.4 (95% CI 2.8–34.1), for coarctation of the aorta being 3.0 (95% CI 1.3–6.6) and for secundum atrial defects being 2.4 (95% CI 1.3–4.4). The OR of risk of anti-hypertensive drug-related pulmonary valve stenosis for treatment initiated after the first trimester amounts to 2.4 (95% CI 1.1–5.4), the corresponding OR for perimembranous ventricular septal defect being 2.3 (95% CI 1.2–4.6) and for secundum atrial septal defect being 2.4 (95% CI 1.3–4.4).4

Although a more intensive haemodialfiltration protocol (including haemodialfiltration at least 6 times a week) appears to be the one that conferred a favourable outcome in five pregnant women with pretreatment creatinine in the range 3.5–7.3 mg/dl (median 5.4 mg/dl), who subsequently gave birth to offspring who developed into healthy infants, the effect of that regime on blood pressure was not documented.5 Accordingly, the remit of future research should include evaluation of the intensity of haemodialysis which best maintains maternal blood pressure in an optimum range and also mitigates the risk of foetal distress attributable to hypotensive episodes. That research would also provide an answer to the vexed question of what the ‘goal’ blood pressure ought to be in the pregnant hypertensive patient who is on haemodialysis.

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Statin therapy, muscle function and vitamin D

Sir,

The observational study of Scott and colleagues1 was noteworthy for finding that statin therapy exacerbates muscle performance and increases falling risk in elderly subjects. This is particularly relevant, since the use of statins has been rapidly escalating in the elderly2 and adequate muscle strength is vital for maintaining independence and quality of life.3 We suggest that vitamin D deficiency might explain much of the observed muscle performance decline and increase in falls among elderly statin-treated patients.

Vitamin D is important for adequate muscle function. The active form of vitamin D, 1,25-dihydroxyvitamin D [1,25(OH)2D] binds to two different vitamin D receptors in the myocyte.4,5 At a genomic level, 1,25(OH)2D binds to the nuclear receptor leading to an increase in de novo protein synthesis; at a nongenomic level, 1,25(OH)2D binds to the cell membrane receptor, rapidly enhancing muscle contraction.

Interestingly, two recent case series reports6,7 suggest that vitamin D insufficiency, serum 25-hydroxyvitamin D [25(OH)D] levels below 30 ng/ml, is associated with statin-induced myalgia. Importantly, the myalgia was reversed with vitamin D supplementation even while continuing statin therapy. Moreover, in the absence of statin therapy, severe myopathy is associated with vitamin D deficiency, serum 25(OH)D levels <20 ng/ml and reversed with vitamin D supplementation.8 Furthermore, meta-analysis has shown that vitamin D supplementation reduces the risk of falls by >20% among elderly ambulatory or institutionalized individuals.9

It is disturbing that vitamin D insufficiency and deficiency have been increasing in the USA over
the past decade. As a result, a majority of the population is now vitamin D insufficient and this state is even more prevalent in darker skinned individuals. Similar trends have been seen in European populations.

Optimal serum 25(OH)D levels for lower extremity function are 40 ng/ml and higher. Since a majority of individuals are vitamin D insufficient, vitamin D supplementation will be necessary to achieve these levels. Oral supplementation with daily cholecalciferol (vitamin D₃) will be adequate to correct most insufficiency states and toxicity is rare when doses do not exceed 10,000 IU daily or serum levels are not >100 ng/ml. Of note, 1000 IU of vitamin D₃ increases serum 25(OH)D levels by ~7 ng/ml.

In summary, it is important for elderly individuals to maintain adequate vitamin D levels for proper muscle performance and fall prevention. The study of Scott and colleagues suggest that maintaining vitamin D adequacy even becomes more critical in the elderly treated with statin therapy. Therefore, we advise measuring serum 25(OH)D levels prior to the use of statins and periodically during treatment, and maintaining levels >40 ng/ml with appropriate supplementation. Finally, statin therapy is expensive and of questionable benefit in the elderly, particularly in the primary prevention of cardiovascular disease, but, vitamin D supplementation is inexpensive and its potential benefits are huge in this population.

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