Testosterone therapy rebuilds muscle in older men

Testosterone is a potential treatment for physical dysfunction due to age-related decreases in muscle mass. These decreases are largely the result of a loss of type II skeletal muscle fibers, and testosterone therapy has been shown to increase muscle mass. A group of US investigators has found that administration of exogenous testosterone results in dose-dependent increase in the number of both type I and type II fibers.

Endogenous testosterone production was blocked in 36 healthy men (aged 60–75 years), who subsequently received testosterone enanthate injections (25 mg, 50 mg, 125 mg, 300 mg, or 600 mg) weekly for 20 weeks. Analysis of cross-sectional biopsies of the participants' thigh muscles taken before and after treatment showed that the number of type I and type II fibers increased dose-dependently. The number of myonuclei and satellite cells also increased dose-dependently (only with the three highest doses); this finding suggests that testosterone promotes entry of myogenic precursor cells into the cell cycle. Further analysis showed that the increased number of satellite cells was the result of satellite-cell replication and activation.

Although these results are highly encouraging, the use of high doses of testosterone to rebuild skeletal muscle in older men is limited by adverse effects. The authors call for further study of the mechanisms involved, in the hope that new targets for anabolic therapy will be discovered.

Original article Sinha-Hikim I *et al.* (2006) Effects of testosterone supplementation on skeletal muscle fiber hypertrophy and satellite cells in community dwelling, older men. *J Clin Endocrinol Metab* [doi: 10.1210/jc.2006-0357]

How to improve BMD in women with anorexia

Miller *et al.* have previously demonstrated that >85% of women with anorexia nervosa have below-normal BMD. They have now shown that the BMD of these women decreases at a rapid rate—approximately 2.5% per year.

The spinal and hip BMD of 75 women who initially had active anorexia (stratified according to oral-contraceptive use, recovery of menstruation, and improvement in weight) was determined during visits a mean of 13.5 months apart.

Miller *et al.* found that BMD of the spine and hip declined annually by a mean of 2.6% and 2.4%, respectively, in women who did not use contraceptives and who did not gain weight or recover menstruation over the course of the study. Women who gained weight showed an increase in hip BMD (independent of recovery of menstruation, $P=0.02$); women who recovered menstruation showed an increase in spinal BMD (independent of weight gain, $P=0.05$). Those who both gained weight and recovered menstruation increased their spinal and hip BMD annually by a mean of 3.1% and 1.8%, respectively. Regression analysis showed that BMD increases were significantly associated with the percentage gain in lean body mass ($P=0.003$), but not with increases in weight or fat mass. In women taking contraceptives, there was no increase in BMD regardless of whether they gained weight or not.

Although it remains unclear whether the effect of menstrual recovery resulted from nutritional improvements or hormones, these results indicate that improvements in both weight (particularly lean body mass) and menstrual function are necessary for overall increases in the BMD of anorexic women.

Original article Miller KK *et al.* (2006) Determinants of skeletal loss and recovery in anorexia nervosa. *J Clin Endocrinol Metab* [doi: 10.1210/jc.2005-2818]

Alendronate limits the effectiveness of teriparatide in combination therapy

Alendronate and teriparatide both improve BMD in osteoporotic patients, and it seems logical that combination therapy with both agents would have a higher efficacy than either of them alone. When this combination therapy was used in two randomized, controlled trials (one by Finkelstein *et al.*), researchers made the surprising discovery that combination therapy was, at best, no more effective than teriparatide alone at increasing BMD. Alendronate even seemed to impair teriparatide's efficacy. Finkelstein *et al.* further analyzed the data from their trial in order to determine whether alendronate inhibits teriparatide's stimulatory effect on bone turnover.