AN *IN VIVO* HUMAN TIME-EXPOSURE INVESTIGATION OF A COMMERCIAL SILVER NANO-PARTICLE SOLUTION. M. A.

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BACKGROUND: The biodistribution, bioprocessing and possible toxicity of silver nanoparticles is receiving increasing attention in human health through greater exposures.

METHODS: To understand whether these concerns are justified, we prospectively studied 3-, 7-, and 14-day exposures to an American Biotech Laboratory 10-ppm (15 ml/day) silver solution in a doubleblind, controlled, cross-over phase design. Healthy volunteer subjects (36, 12 each time-exposure), underwent complete metabolic, blood and platelet count, urinalysis tests, sputum hyperresponsiveness and inflammation evaluation, physical examinations, vital sign measurements, and magnetic resonance imaging of the chest and abdomen at baseline and end of each phase. Diet was not controlled. Silver serum and urine quantization was determined by inductively coupled plasma mass spectrometry (NMS Labs). Significance in individual laboratory values was determined by any value being 2 x ULN or 4 SD from
the mean and by clinical judgment. Mixed effects linear and logistic regression models compared the mean effect to the normal reference range control limits. MRI morphology changes were qualitatively described.

RESULTS: No clinically important changes in any metabolic, hematologic, or urinalysis measure identified were determined. No morphological (or structural) changes were detected in the lungs, heart (cardiac function) or abdominal organs. No changes were noted in sputum
reactive oxygen species or in pro-inflammatory cytokines.

CONCLUSION: *In-vivo* oral exposure of a commercial 10-ppm silver nano-particle solution over 3-, 7-, and 14-day exposures does not exhibit clinically important changes in metabolic, hematologic, urine, vital sign changes, physical findings or imaging changes visualized
by MRI. Further study of increasing time-exposure, dose, and additional organ systems, including cytochrome P-450 enzymes, is warranted.