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Correction to "Inhaled Nanoparticles Accumulate at Sites of Vascular Disease"

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The authors submit the following corrections. A mislabeling of the units was found in Figure 2D. The *y*-axes of both graphs should read: "concentration of gold (ng gold/L)" not "(ng gold/mL)". Similarly, in Supplementary Figure S4 the urine concentration on the *y*-axis should also read: "concentration of gold (ng gold/L)".

This error affects the estimate of % mass translocation in the Discussion, which also contained inconsistencies. We have now corrected these errors and refined our exposure estimates for this calculation. Thus, we would like to revise the following text on page 4546:

"Based on the exposure characteristics of our first study (2 h exposure of ∼116 $\mu g/m^3$ under light exercise), we calculate the total inhaled dose of particulate to be ∼690 mg. If ∼80 μg of gold was cleared by the kidneys over 24 h (average volume of urine collected: 2.4 L containing 35 ng/mL), and, therefore, if this was the sole route of clearance, we estimate that at least 0.2% of inhaled gold nanoparticles translocated from the lung into circulation".

This should be replaced with:

"Based on the exposure characteristics of our first study (2 h exposure of ∼116 $\mu g/m^3$ intermittent rest [6 L/min for 4 × 15 min] and moderate exercise [47.5 L/min for 4 × 15 min]), we calculate the total inhaled dose of the particulate to be ∼383 μg. If ∼84 ng of gold was cleared by the kidney over 24 h (average volume or urine collected: 2.4 L containing 35 ng/L; Figure 1D), we estimate that at least 0.02% of inhaled gold nanoparticles translocated from the lung into the circulation".

We emphasize that this calculation is for illustrative purposes and represents only a defined 24 h period in time. The estimate is likely to be conservative and does not take into account the proportion of alveolar deposition and the slow return of respiratory rate to resting levels after exercise and is based on the assumption that the urine is the sole route of clearance.

While this estimate is an order of magnitude lower than that stated in the original manuscript, the proportion of translocated particles still fits with prior findings. Early studies in rodents provided rough estimates that <1% mass of nanoparticles with a diameter of <50 nm will translocate.[1] Subsequent studies broadened this range from 0.01 to 10%, although estimates are most frequently around 0.3% or less for a given tissue at 24 h post-exposure.[2−11] Studies in man are hampered by technical limitations,[12,13] although, on the assumption that translocation can occur in man, current findings suggest a very low rate of translocation.[14−16] Thus, the estimate of 0.02% translocation in the present study concurs with that of previous work.

Differences in the species, method of exposure, particle size, particle physicochemistry, post-exposure sampling period, method of measurement and tissue sample(s) used, all make direct comparisons between these studies challenging. In most instances (especially where values are close to the threshold of detection), the relative amount of gold in exposed *versus* non-exposed tissues (within the same study) has arguably greater value than the actual concentration of gold *per se*. However, the calculation has qualitative value in that it confirms or strengthens several key messages about the translocation process:

(1) A very low proportion of nanoparticles translocate from the lung to the blood in both animals and man.
(2) The body has several routes of clearance of translocated nanoparticles (including, but not limited to, the urine and *via* the liver) that will affect systemic levels of nanoparticles. Nevertheless, translocated nanoparticles accumulate in several tissues. The individual biokinetics of these routes requires further research.
(3) Particles are retained in the lung for long periods of time, thus, there appears to be an ongoing slow translocation of low amounts of nanoparticles into the blood (from the lung and/or other organs they may have originally accumulated in).

These corrections do not affect any other findings of the paper or the conclusions drawn. The important observation in the current study is that translocated nanoparticles reach and accumulate at areas of disease that may be most susceptible to their physicochemical properties. Thus, the preferential accumulation in regions of susceptibility suggests that translocated nanoparticles could cause significant biological actions that promote the disease process.

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