Medical Surveillance for Nanomaterials

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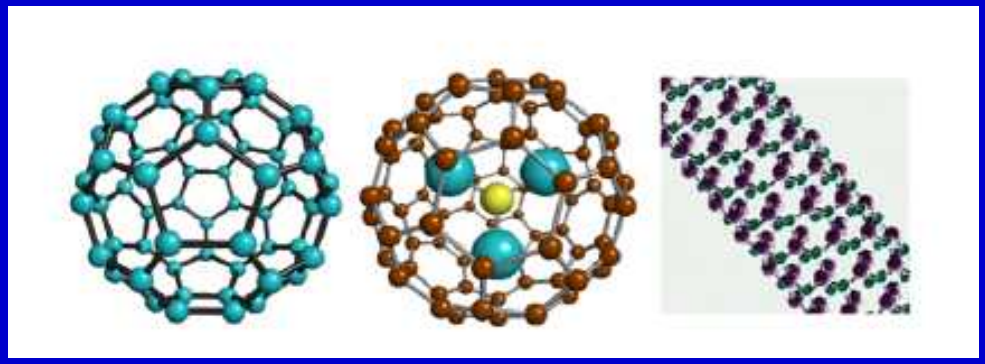
What is nanotechnology?

The ability to understand, control and manipulate matter at the level of atoms, or on the scale of 1 to 100 nanometers, in order to create materials, devices, and systems with fundamentally new properties and functions because of their small structure.



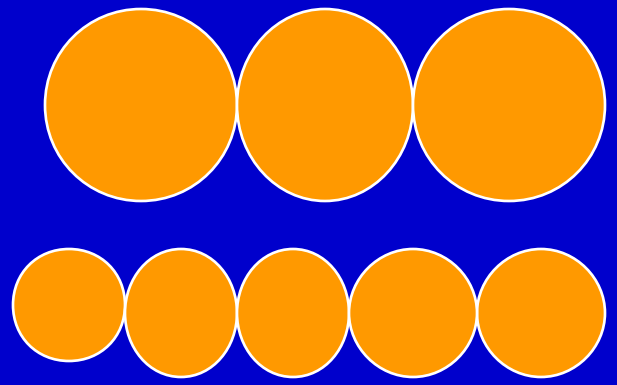
Size of Nanoparticles Relative to Cells & Components

	nm
White blood cell	~10,000
Bacteria	1,000 – 10,000
Materials internalized by cells	<100
Viruses	75 – 100
Nanoparticles	1 – 100
Protein	5 – 50
Quantum dots	8
DNA (width)	2
Fullerenes	1
Single atom	0.1

(Schulte, 2006)

Particle Number and surface area for area for 10 mg/m^3 airborne particles

Particle Diameter (µm)	Particles/ml of air	Particle Surface area (µm^2/ml of air)
2.0	2	30
0.5	153	120
0.02	2,390,000	3000



Large particle

Small particle

(Moss, 2006)

Nanotechnology: Challenges to Occupational Health

Nanoparticles may have different toxicokinetic and toxicodynamic properties than larger particles

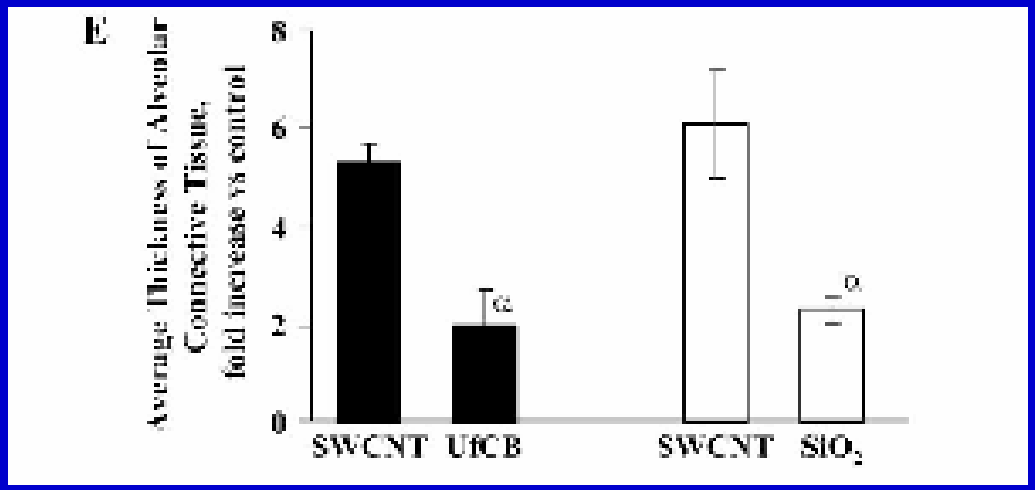
Appropriate measurement of nanomaterial exposure may require new metrics (e.g. surface area rather than mass), and advanced technology (e.g. electron microscopy)

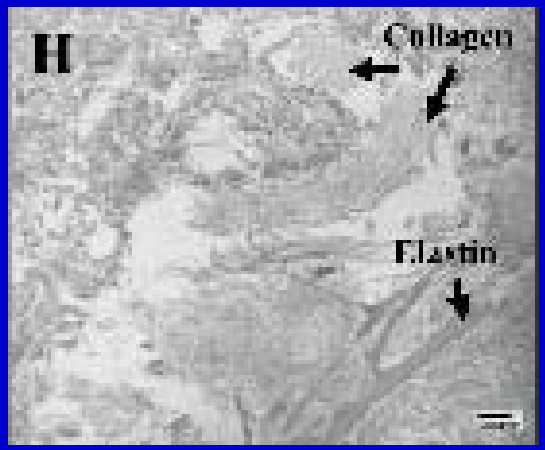
"Safe" or "Permissible Exposure Levels" are uncertain -- Standards created for larger particles may not be suitable for nanoparticles

Faced with workplace exposure to materials of uncertain but possible toxicity that are challenging to measure, it is prudent to:

- **Exercise strict exposure controls**
- **Enumerate and track exposed workers**
- **Characterize baseline health status using available, standard methods**
- **Conduct voluntary epidemiological research on exposed populations**

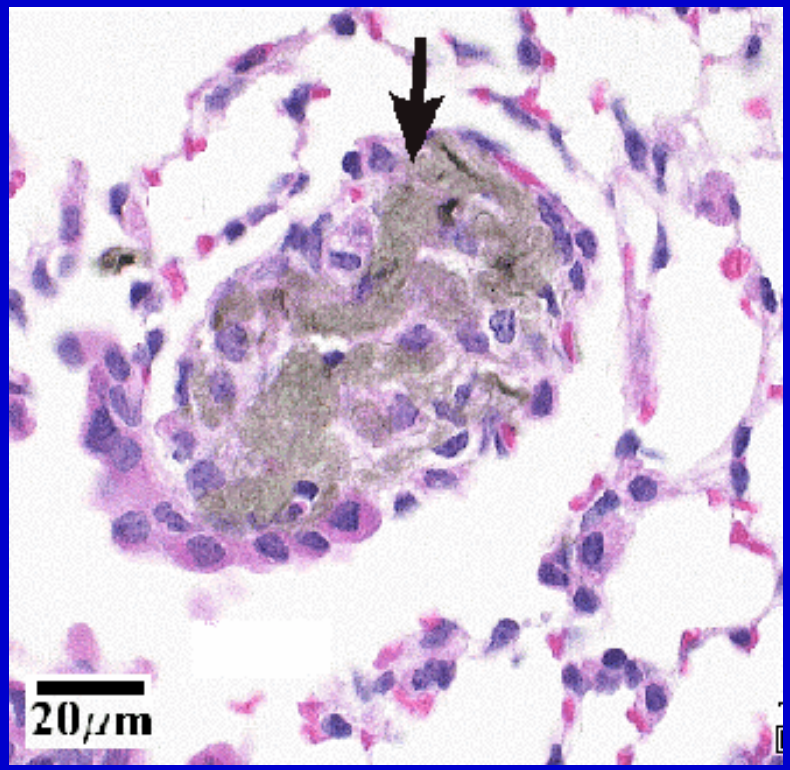
Lung deposition of carbon nanotubes in mice resulted in alveolar wall fibrosis. This effect was not seen with carbon black or crystalline silica.

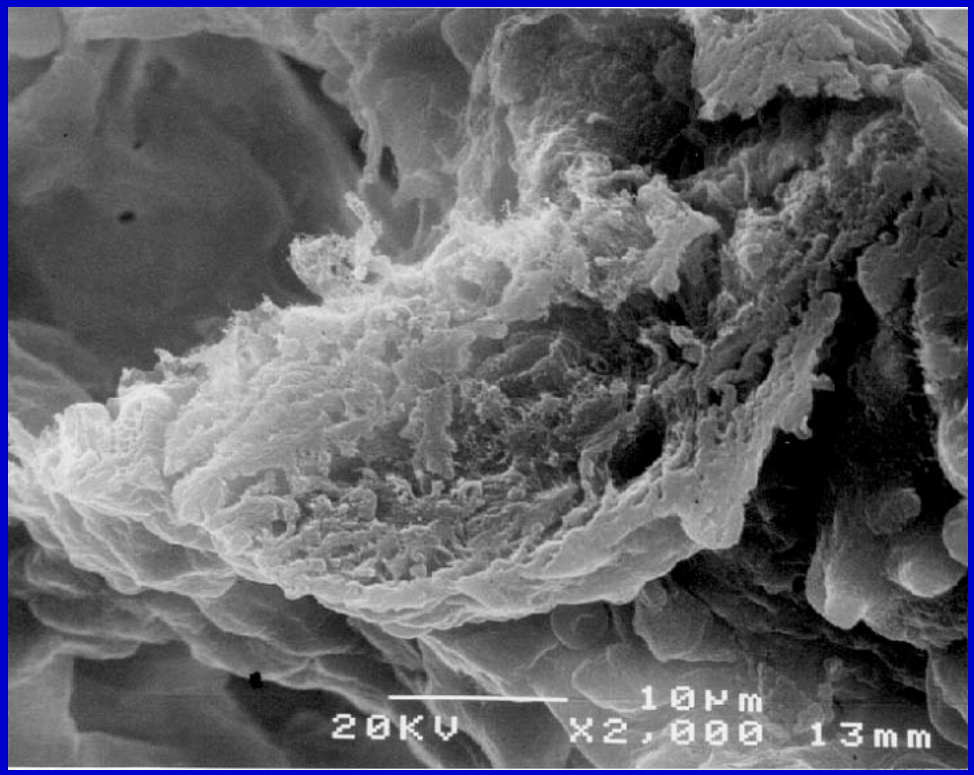




(Shvedova et al, 2005)

Carbon nanotubes (CNT), but not carbon black, induced pulmonary granulomas.

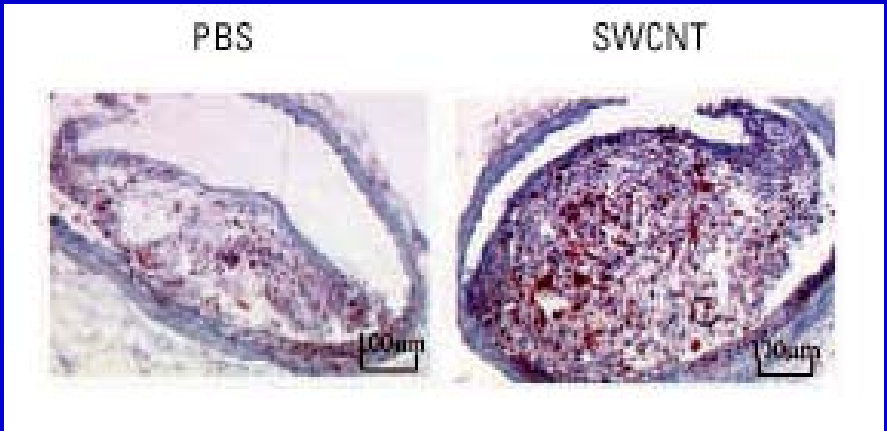


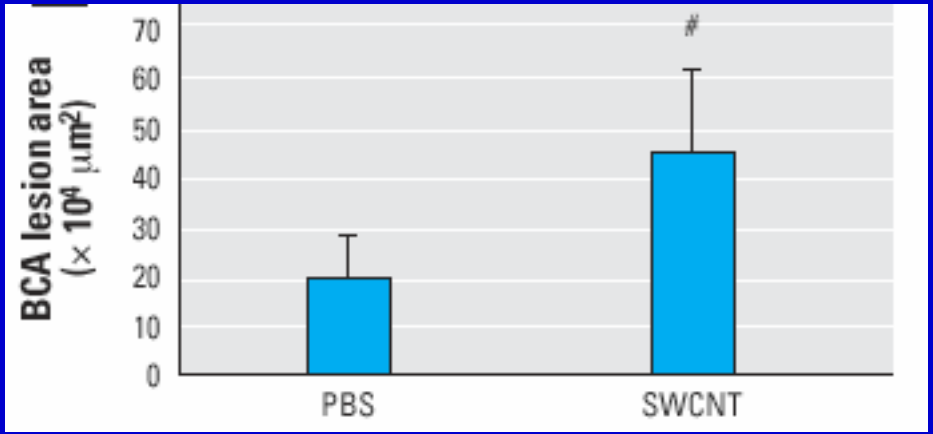


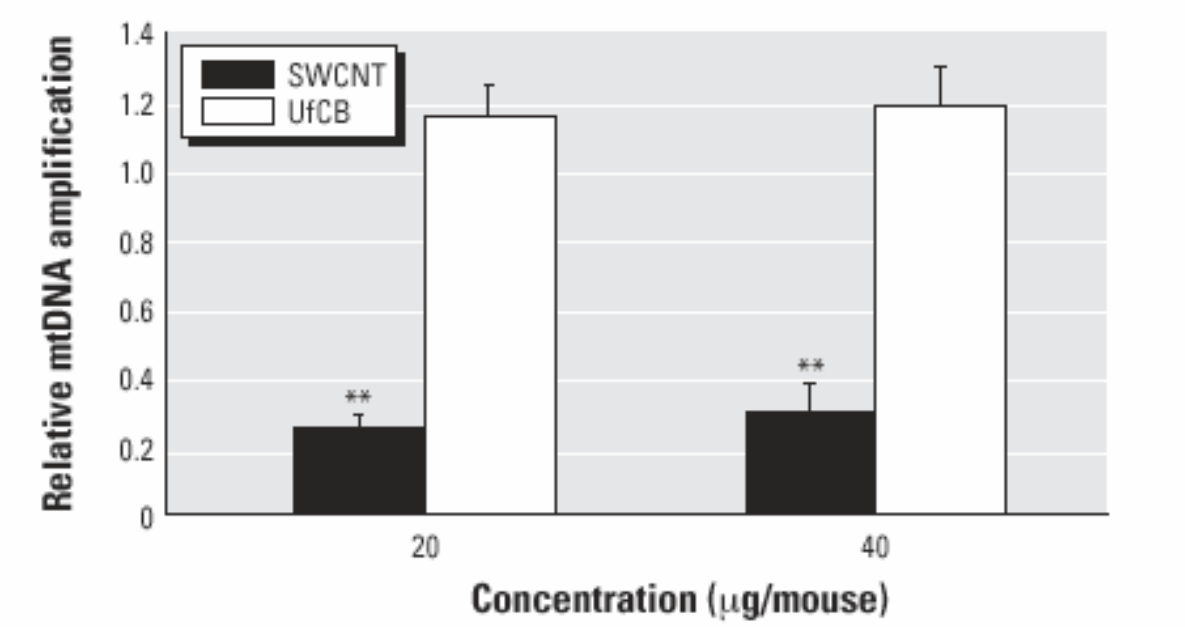
The lung dose of CNT was equivalent to what a worker might inhale after 20 days at the OSHA PEL for carbon black (graphite).

(Shvedova, 2005)

Mice exposed to CNT via the lung developed increased atheromatous plaques in their circulatory system.







(Li et al, 2007)

Medical Surveillance for Pulmonary Endpoints

Chest x-ray	**Insensitive, esp. for granulomatous lung disease;** **Nonspecific;** **Interpretation: limited reproducibility**
Spirometry	**Insensitive for interstitial / gran lung dz** **Can be hard to standardize**

Potential Future Modalities:

Serum biomarkers: KL-6; Neopterin; ACE -phenotype adj.

Imaging: High Resolution Chest CT; spiral CT

Exercise Oximetry

Potential Screening Tests for Cardiovascular Disease/ Atherosclerosis

- Resting electrocardiogram?
- Exercise testing? (including stress echo)
- Chest CT / calcium scores?
- Gated CT of coronary arteries?
- Magnetic Resonance Imaging of coronary arteries?
- Heart rate variability on electrocardiogram?

Nanotechnology Worker Exposure Registries: A Rational Starting Point

Multi-company/ industry-wide registries preferred to increase enrollment number; allow for longitudinal tracking with job changes

Data elements: demographics; job/task duties; type(s) of nanomaterial encountered; tabulated by dates of employment at specific facilities

Exposure measurements (if available):
particle mass, count, and surface area

Engineering controls; personal protective equipment

Medical data collected because of other OSHA regulations or surveillance programs (e.g. CXR, spirometry, questionnaires) could be included in the Nanotechnology Exposure Registry.

However, at present, no specific medical tests have been validated to be of practical, preventive value for nanotechnology workers.

A Nanotechnology Worker Exposure Registry will facilitate voluntary epidemiological research that uses emerging biomarkers or investigates potential adverse health effects.

Contemporaneous exposure data collected for the registry will avoid pitfalls of retrospective dose reconstruction.

Aggregated data analysis may allow early detection of trends, increasing statistical power.

Voluntary, confidential, epidemiological research utilizing passive collection of health outcome data should be considered:

- **Diagnostic codes (e.g. "myocardial infarction", "sarcoidosis") collected from disability claims, return to work questionnaires, health insurance claims.**
- **Cause of death data from death certificates or death benefit programs**

Information collected in a Nanotechnology Worker Exposure Registry created now will facilitate targeted medical surveillance and risk notification programs in the future.