



Medical Surveillance and Nanotechnology Workers

Peter D. Lichty, MD MOH FACOEM
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Outline



- **Principles of Medical Surveillance**
- **Sensitivity and Specificity of Medical Tests**
- **Variability of Medical Tests**
- **Biologic plausibility for engineered nanomaterial health effects.**
- **Routes of exposure**
- **Describing a specific nanoparticle**

ACOEM Principles of Medical Surveillance



- **ACOEM: American College of Occupational and Environmental Medicine**
- **The primary purpose of any medical surveillance program is the early detection of an adverse health effect, at a time when intervention can lead to disease reversal or cessation of progression.**
- **The medical tests used for surveillance should be reasonably reliable detectors of early disease with good sensitivity and specificity. They should be simple and cost-effective to administer, and present little risk or inconvenience to workers.**

ACOEM Principles of Med. Surv.



- **Additional benefits of a surveillance program include the opportunity to educate workers about risks they face and the opportunity to do research into early predictors of disease. Finally, a surveillance program can even stimulate employers to add engineering or administrative controls to the workplace (e.g., audiometry in hearing conservation programs).**

Example: Hearing Tests



	Audiometry Characteristics	Comment
Health Effect	Noise-induced Hearing Loss	Multiple other causes of hearing loss
Intervention Yields	Check on PPE, education	Cannot reverse SNHL.
Test Quality, Variability	Good, moderate variability	Seasonal variations
Test Cost	Minimal	Large population
Test Risk	None	

Other Regulated or Recommended Exams



- Exams that must be offered by regulation:
 - 17 OSHA substance-specific exams (e.g. asbestos). 5 other exams: Hazwoper, BBP, hyperbaric, respirator, noise.
- Exams that must be passed to qualify for a job, by regulation:
 - Department of Transportation driver physicals, drug tests.
- Exams that must be taken to qualify for a job, by regulation:
 - Hearing tests (Employer “shall obtain” test).
- Exams recommended by other groups, usually voluntary, sometimes swept into regulations by reference (e.g. crane exams).

Other Workplace Examinations



- **Examinations after laboratory spills or exposures (OSHA 1910.1450 “Occupational exposure to hazardous chemicals in laboratories.”)**
- **Preplacement examinations – Americans with Disabilities Act limits to:**
 - Post-offer examinations**
 - Geared to ability to perform essential functions, and need for reasonable accommodations.**
 - Exclusionary criteria must be job-related and consistent with business necessity.**
 - All job candidates get same exam.**

Other Exams



- **Voluntary Periodic Examinations – assess health risks, screen for disease, health promotion focus.**
- **Termination Physicals – assess health before retirement or leaving employment.**

What Standards Apply to Nanotechnology?



- **Could be covered by a substance-specific exam due to exposure levels of substance mass or precursors or byproducts.**
- **Could be covered by process exposure, such as noise, confined space.**
- **In research, will be covered by 1910.1450, which requires medical consultation and examination when:**
 - Signs or symptoms associated with potential exposure,**
 - After a spill, or**
 - Monitoring measures exposure above TLV or PEL.**

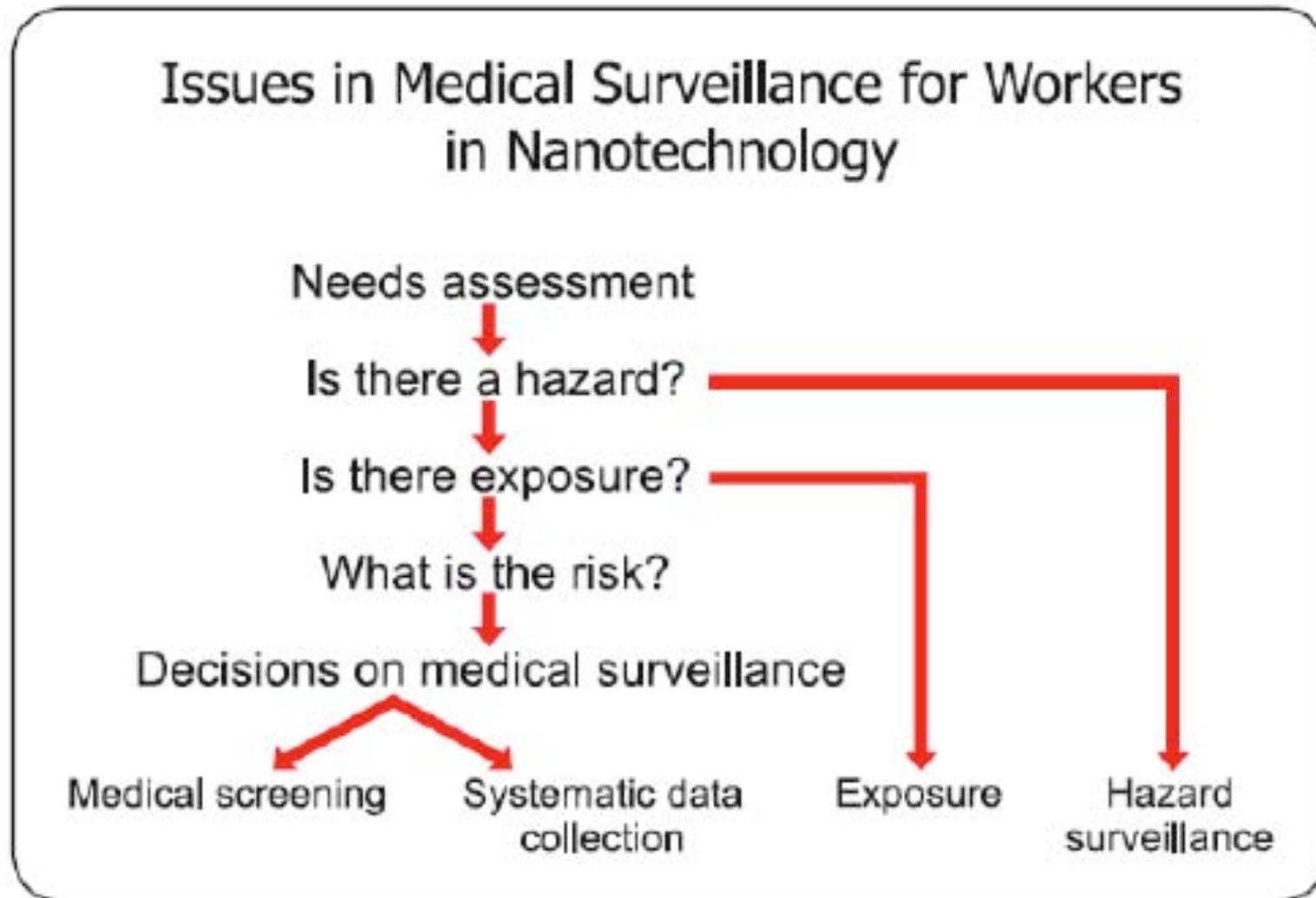
Lab Standard Definitions



- ***Laboratory*** means a facility where the "laboratory use of hazardous chemicals" occurs. It is a workplace where relatively small quantities of hazardous chemicals are used on a non-production basis.

Laboratory scale means work with substances in which the containers used for reactions, transfers, and other handling of substances are designed to be easily and safely manipulated by one person. "Laboratory scale" excludes those workplaces whose function is to produce commercial quantities of materials.

NIOSH Surveillance Flowchart



Is There a Hazard?



- **Particle characteristics:**
 - composition, size, shape, surface characteristics, charge, functional groups, crystal structure, and solubility.
- **Where are the particles?**
 - which jobs or processes involve the production or use of engineered nanoparticles?
 - Employers should identify and document the presence of engineered nanoparticles in their workplaces and the work tasks associated with them.
 - Are the particles dispersible? Will the process disperse them?

How is the Risk of Unknown Effects Managed?



- **Once we have recognized potential exposures, we should determine appropriate actions for minimizing them:**
 - implementing engineering controls,
 - employing good work practices,
 - and using personal protective equipment
- **Examples:**
 - Gloves
 - HEPA filtering air
 - Enclosure

Is There Exposure?



- **Highest risk of workplace exposure is probably airborne nanoparticles.**
- **Measuring airborne nanoparticles is not a trivial task.**
 - **Cannot differentiate engineered from background nanoparticles.**
 - **Indoor background 10,000 per cc, or 30 million per breath.**
 - **Outdoor background is even higher.**
- **Industrial hygiene judgment and a nanoparticle counter will likely identify highest exposure areas.**

Is Medical Surveillance Appropriate?



- **If unknown effect:**
 - Standard examinations may miss it,
 - We don't know if effect is reversible,
 - We don't know if tests are reliable,
 - There is no opportunity to educate.
- **“Nonspecific medical testing could have negative consequences including adverse effects of the tests such as radiation from chest radiographs, unnecessary anxiety from false positive screening tests, and the cost of additional diagnostic evaluations.” (NIOSH CIB draft).**

What Tests Are Available?



- **There is no clinical test to measure:**
 - Transdermal nanoparticle absorption
 - Transneural nanoparticle absorption
 - Gastrointestinal nanoparticle absorption
 - Respiratory nanoparticle absorption
- **Other respiratory tests are severely limited**
 - Spirometry detects late effects, variability $\pm 7\%$, relatively insensitive.
 - Bronchoscopy and lavage is too invasive.
 - Exhaled nitrous oxide is experimental measure of inflammation.

NIOSH Draft CIB on Nanotech Workers



- **“Insufficient scientific and medical evidence now exists to recommend the specific medical screening of workers potentially exposed to engineered nanoparticles.”** (Executive Summary, December 2007)
 - Take prudent measures to control workers’ exposures to nanoparticles.
 - Conduct hazard surveillance as the basis for implementing controls.
 - Consider established medical surveillance approaches to help assess whether control measures are effective and identify new or unrecognized problems and health effects.

NIOSH Conclusions



- **“Inherent in all criteria for medical screening is that the specific disease endpoint(s) must be known to allow for test selection.”**
- **“At this time, no health outcomes that have been determined to be sentinel events are related to engineered nanoparticle exposures.”**

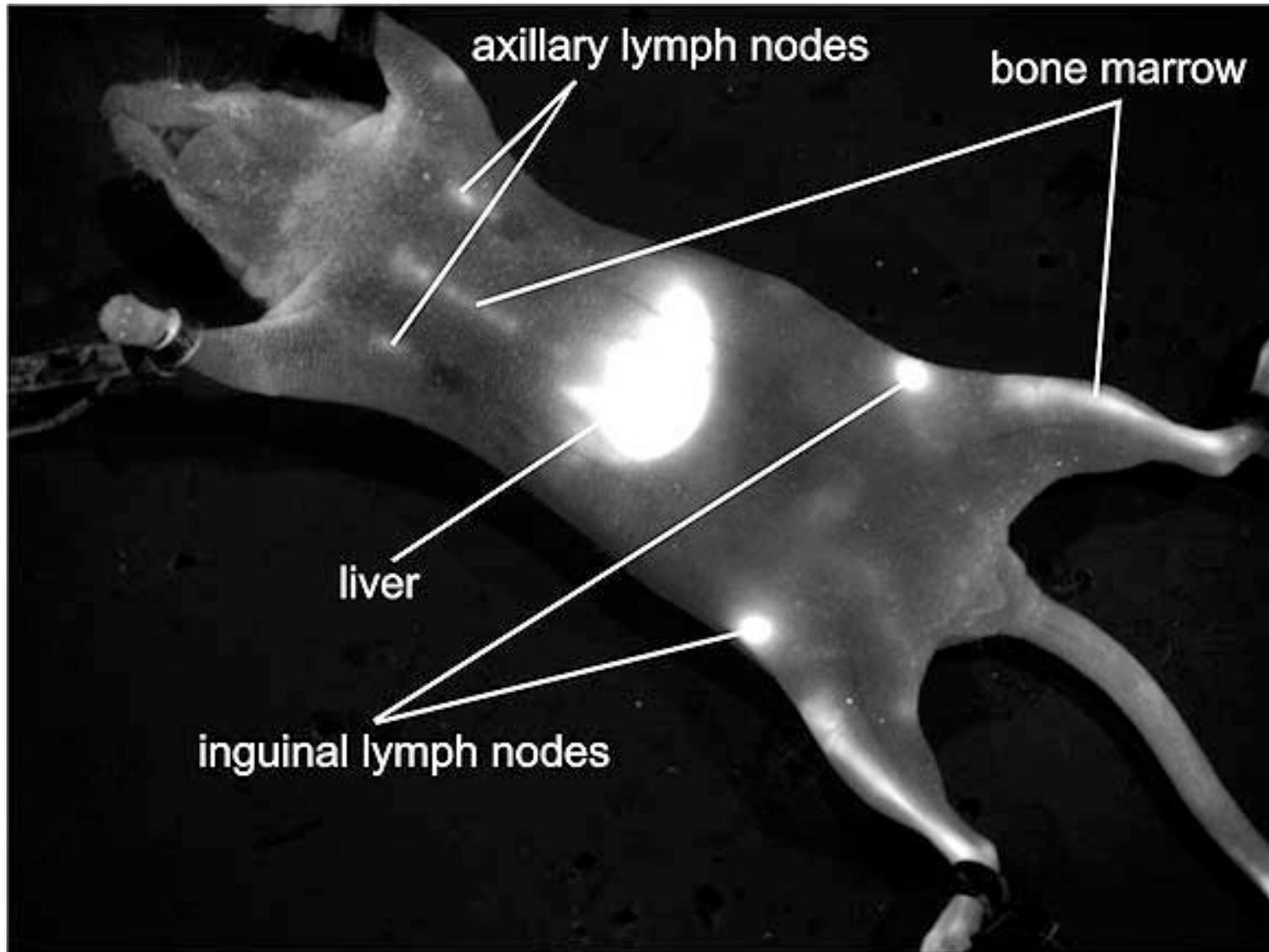
Possible Future Tests



- **Measure body burden of engineered nanoparticles.**
- **Measure excretion of engineered nanoparticles**
- **Measure skin content of nanoparticles.**

- **Initial development of these tests will likely occur in animals, then proceed to human experimentation.**

Quantum Dot Mouse



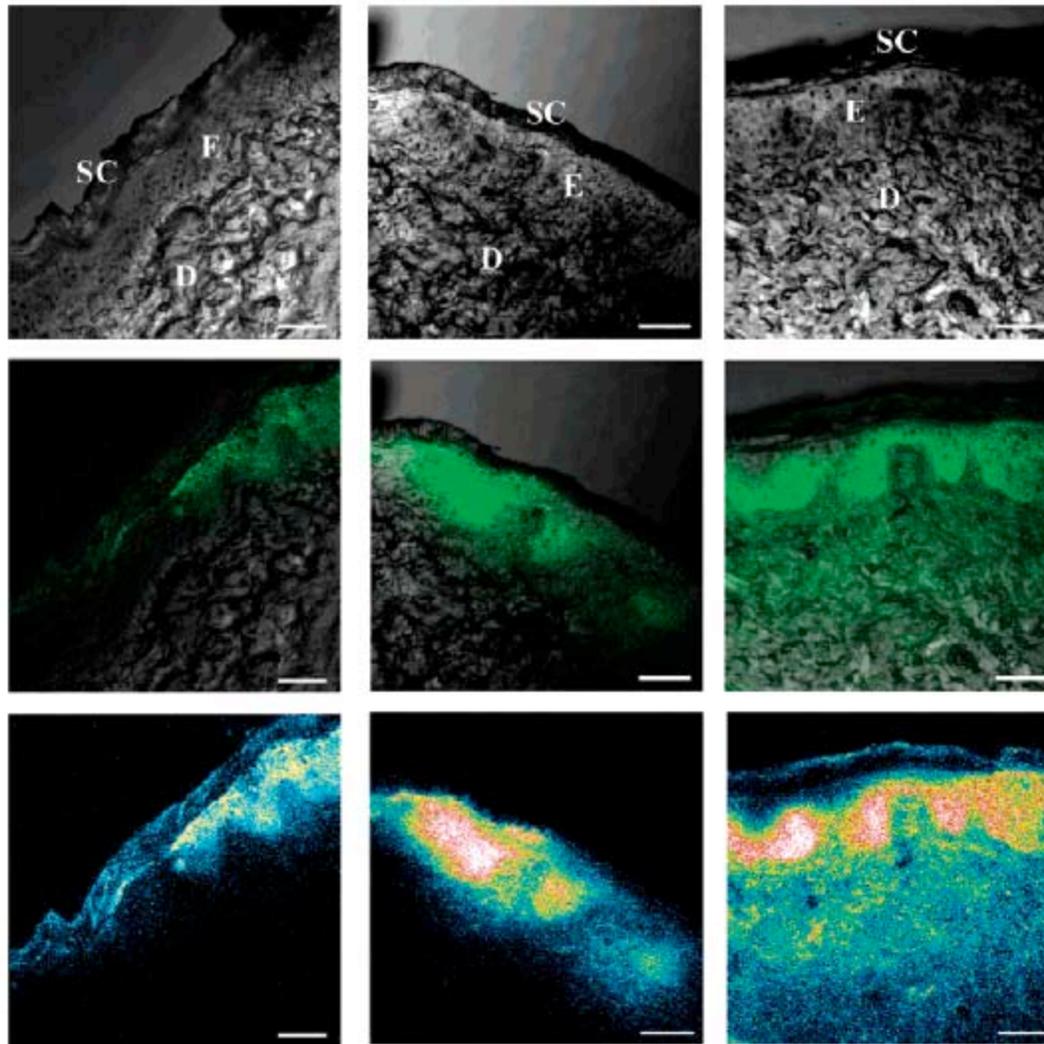
Fullerene Skin Penetration with Flexion



Control

60 min Flex

90 min Flex



Peptide-coated
fullerenes do
penetrate the skin
following flexion
and extension.

Jillian G. Rouse,^{†,‡}
Effects of Mechanical
Flexion on the
Penetration of
Fullerene Amino
Acid-Derivatized
Peptide Nanoparticles
through Skin
NANO LETTERS
2007, Vol. 7, No. 1
155-160

Summary



- **Current knowledge does not provide an evidence-based medical surveillance strategy for engineered nanoparticle workers.**
- **General health monitoring may or may not catch any health effects.**
- **Nonspecific measures of inflammation may be fruitful if exposures are high enough.**
- **There is no reason to think that all engineered nanoparticles will have the same health effects, or the same surveillance strategy.**
- **Close monitoring of engineered nanoparticle toxicity studies is warranted.**