## Concepts in the Inhalation Toxicity of Fire Suppressants: Pneumotoxicity

**Edgar C. Kimmel and Robert L. Carpenter**

Establishing toxicity and evaluation of potential health risk associated with use of an agent is the predicated on establishment of the fundamental dose/response relationship for that agent. Obviously there is a broad spectrum of possible biological responses to agents in general, however there also is a broad spectrum of responses associated with exposure to specific agents. Assessment of potential toxicity and health risk becomes (particularly when risk/benefit analysis is required) an issue of determining what are the pertinent biological responses upon which to base risk assessment. Historically. much of the focus of toxicity evaluations and subsequent health risk assessments have been based on mortality. Because mortality is a dichotomous response its use as toxicity endpoint is straight forward. However, with regard to health risk/benefit analysis mortality as an end point is problematic in that significant health risk can be accrued long before possible mortality is of concern. Consequently toxicologists and related health professionals have begun to refocus their efforts on system, organ and tissue level responses , as a basis for risk assessments. Thus the risk assessment process now must consider a variety of biological responses as well as a continuum within a given response. Never-the-less, the fundamentals of the dose/response evaluation are the foundation of toxicity determination and health risk assessment. The first portion of our presentation will focus dosimetry factors, their interrelationships and how they influence potential toxicity and health risk Responses of the respiratory system, interrelationship between responses and how they impact on risk assessments associated with fire suppressants are topics the latter portion of this presentation.

### Inhalation Dosimetry

Determination of dose via inhalation is more complex than for other common routes of exposure. The lung represents the largest single surface area of the body which is in possible direct contact with the external environment. Access to this surface area is not passive; the lung is brought into contact with the external environment via the act of breathing. Dose via inhalation is a function of both concentration of the agent and ventilation. Therefore the depth and rate of breathing are determinants of dose via inhalation. Because of the structure of the lung and the nature of ventilation dose to the lung as well as the rest of the body is also a function of deposition and retention in the lung. Deposition and retention being factors of time course of contact with the lung tissue as well as the rate at which material is taken up by lung tissues. Deposition and retention in the lung is a function of the physical and chemical characteristics of the agent. . Furthermore the magnitude of deposition and retention as well as the potential impact of deposition and retention of inhaled agents is within lung site specific. Although numerous factors apply, relative water solubility is the predominating factor determining deposition and retention in the lung for gases and vapors. Aerosol deposition and retention has numerous other physical and chemical determinants each of which can assume a predominant role under given circumstances.. The interaction of the

vapor and gas phase constituents with aerosol phase constituents in complex atmospheres also will be addressed.

These same factors are largely those that bear a direct influence on fire fighting efficacy and design of fire fighting systems; forming a basis for the integration of health risk concerns with those of the fire control engineer.

**Pulmonary Response.**

With renewed focus on system, organ, and tissue response in health risk assessment the lung and respiratory system are naturally a point of focus for inhalation toxicology concerns. The lungs and respiratory system represent not only the most common route of entry into the body for most environmental agents but are often the primary target organ. As noted the lung is the largest as well as the most readily penetrable surface of the body that can be brought into direct contact with the external environment. The respiratory system and lungs are far more complex than is routinely acknowledged. Likewise there are many more functions of the respiratory system beyond its generally recognized primary function of gas exchange. Thus there are a multitude of potential responses of the lung to inhaled agents and indeed often multiple responses. Each distinct pulmonary response has its own continuum and distinct responses are usually interrelated. The type and extent of each response and the level of interaction between responses are often directly related to dosimetry factors noted above. Because of the multiplicity of possible responses of respiratory system issues of chronicity (acute vs chronic) are issues of response immediacy and duration as well as of exposure duration. Acute and chronic attributes of the exposure and response are interrelated in a variety of manners. A fundamental understanding of these interactions is important to a thorough understanding of the potential pulmonary toxicity of an agent as well as the determination of health risk associated with use of that agent. The nature of the potential response and related issues is often a function of the manner in which that agent is deployed. Consideration of the type and time course of pulmonary responses to an agent are an integral part of factoring potential health risk factors into fire fighting systems and strategies.

# Concepts in the Inhalation Toxicity of Fire Supressants

## OR

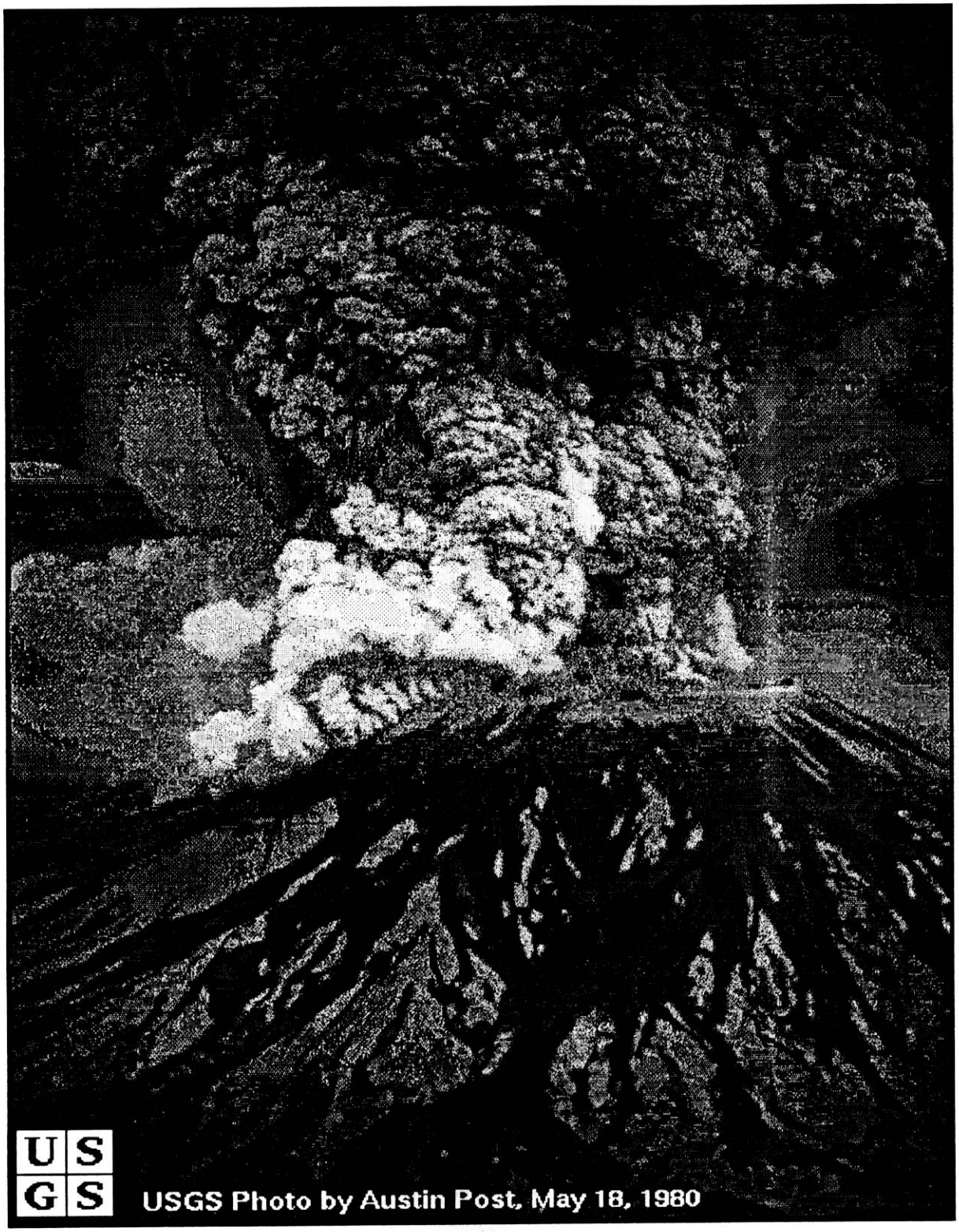
## What You Need to Know About Inhaled Particles: Particle Size and Lung Response

**R.L. Carpenter & E.C. Kimmel**

**Naval Medical Research Institute - Toxicology**

# AEROSOL TOXICOLOGY
## Depends upon

- **Particle properties**
  - **size distribution**
  - **composition**
- **Gas composition**
  - **innocous effect → promoting toxic effect**
  - **noxious effect**
- **Interaction between these phases**



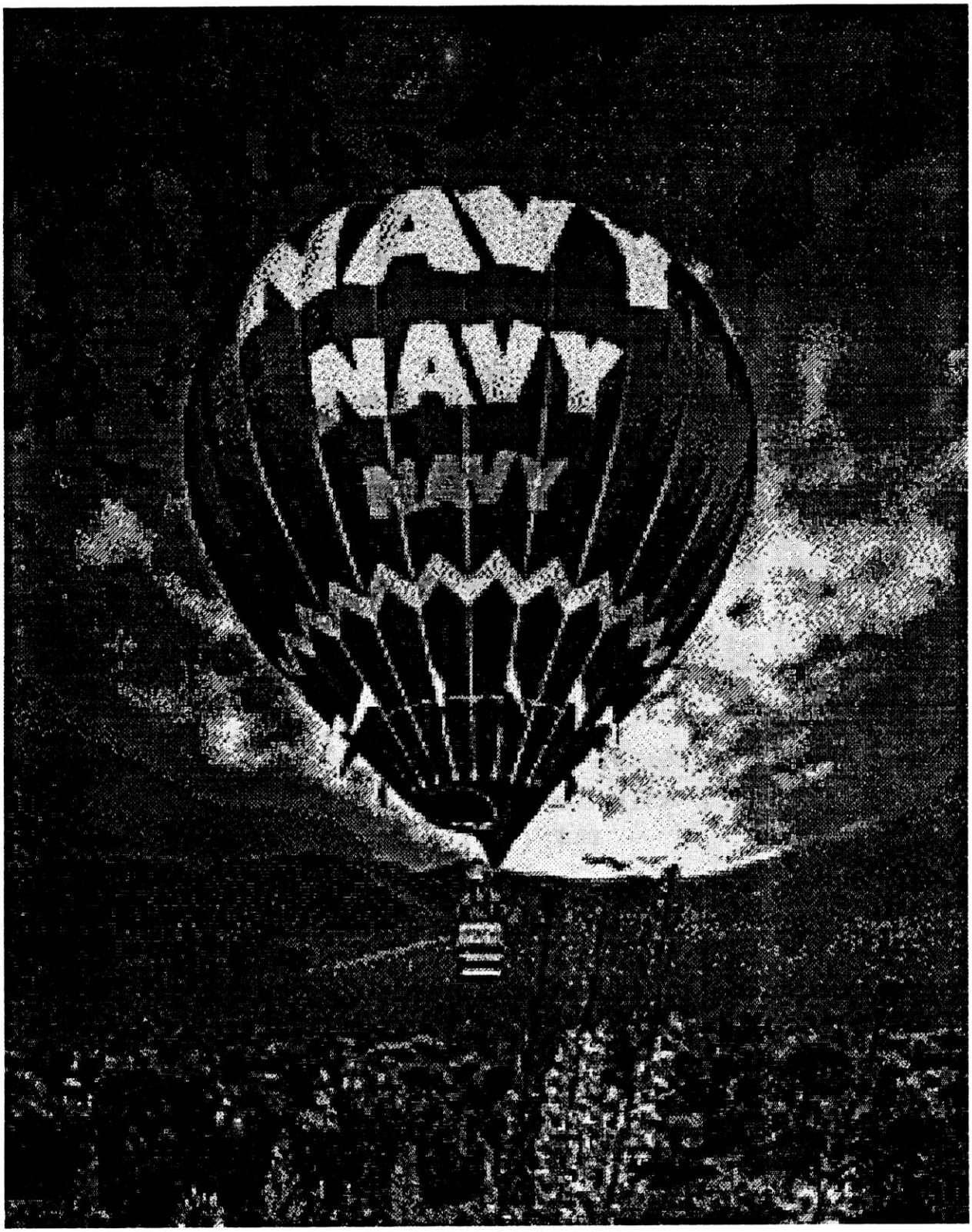

# a well known aerosol

# FACTS ABOUT AEROSOL PARTICLES

- 100 fold range of particle diameter is common
- commonly used size unit
  - micrometer (μm) = 1 x $10^{-6}$ meter
  - mass median aerodynamic diameter (MMAD)
- 80% of particles > 2.5 μm MMAD deposit in the nose
- 10 % of particles < 2.5 μm MMAD deposit in the deep lung

# WHY ARE SO FEW PARTICLES SO IMPORTANT?

- Particles stay in lung for a long time
  - accumulate over time
  - can cause significant lung damage
  - dissolve and leave lung
- Varied ways particles can be toxic
  - intrinsic chemical toxicity (composition)
  - carriers for gas/vapor phase adsorbed on the surface (change in site)
  - cause multiple effects simultaneously




# aerodynamic diameter

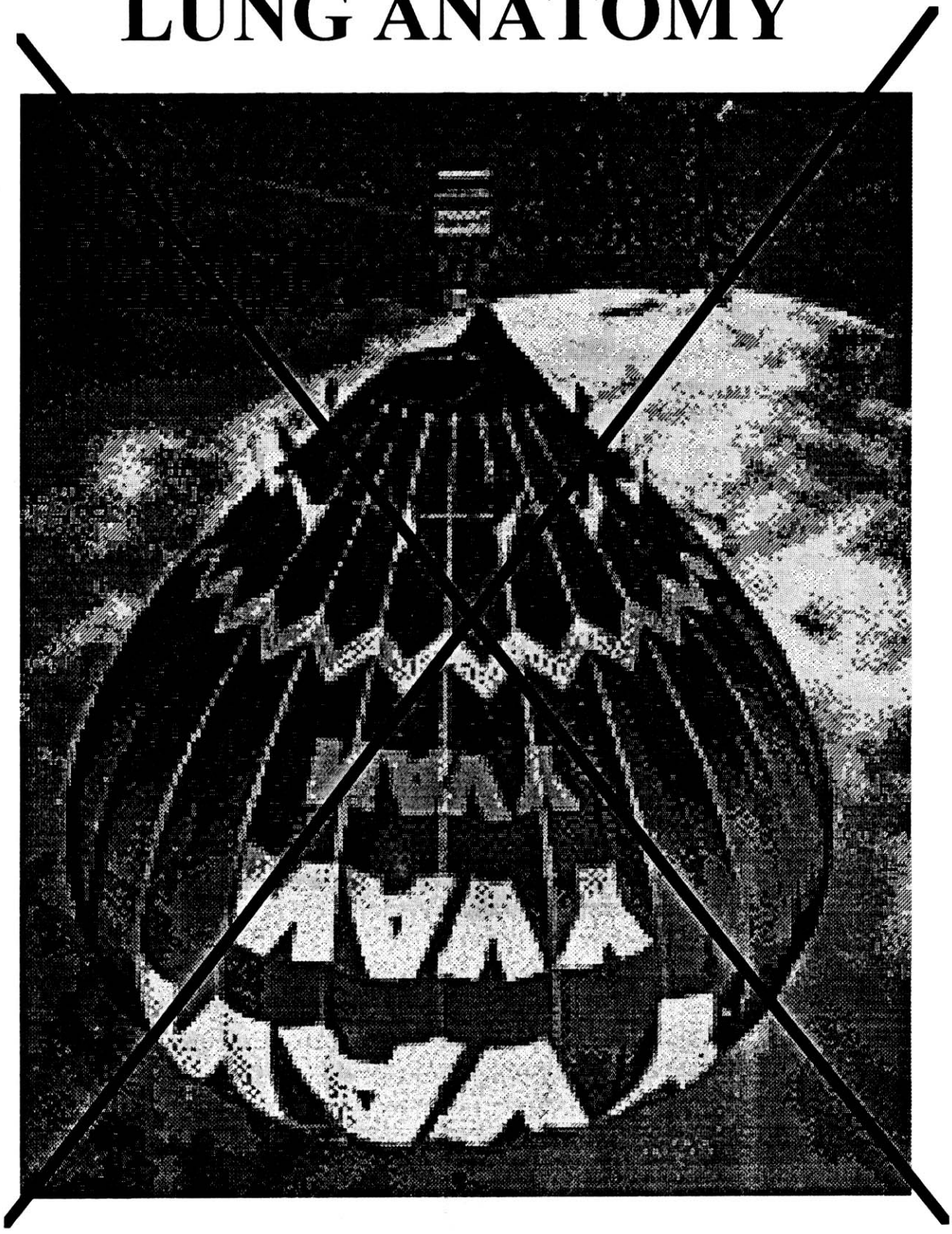
# PARTICLE BEHAVIOR FACTORS

- **Moving target toxicity- change size & shape**
- **Can be re-entrained - long residence time**
- **Difficult to monitor**
  - **form on the fly "here today gone tomorrow"**
  - **sizes vary, 1 x $10^{-3}$ to 1 x $10^{2}$ = 15 orders of magnitude in particle mass**
  - **concentrations vary about 14 orders of magnitude**
- **Chemical heterogeneity & reactivity**

# LUNG BIOLOGY/FUNCTION & aerosols

- **Largest body surface area - 70 $m^2$**
  - **EXTERIOR - expends energy to for direct contact with outside**
  - **Very thin - 8 - 12 μm**
- **Specialized defense mechanisms**
  - **Toxicity targets - damage/ repair process balance**
- **Series of 'wind tunnels" leading to thin bags - structure accounts for aerosol toxicity**
  - **fluid mechanics as a determinant of dose**
  - **dose is a function of depth of breathing**

# LUNG ANATOMY

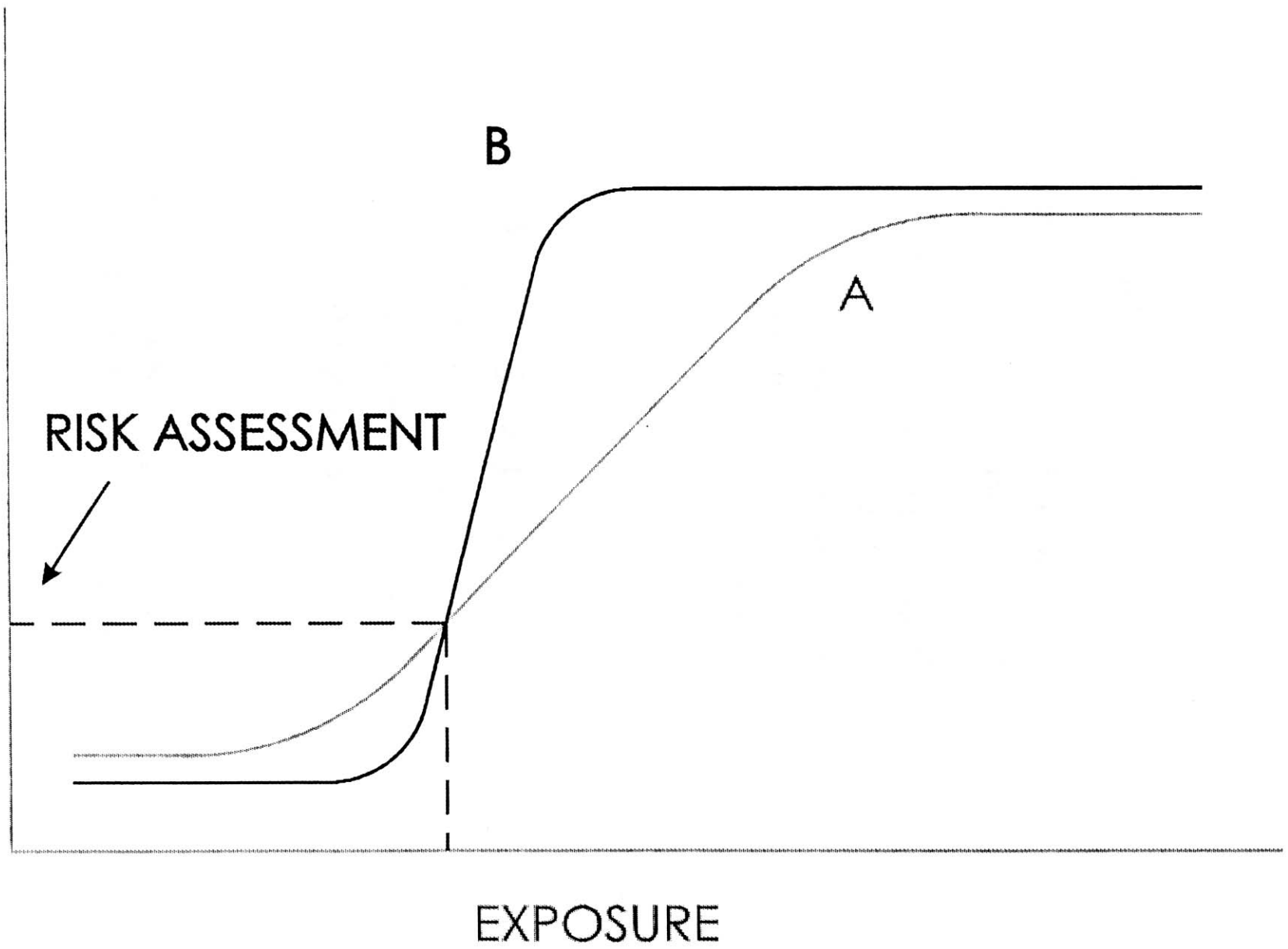


# LUNG TOXIC RESPONSES

- **Direct and indirect damage or both**
- **Variety of responses with varying severity**
- **Responses are non-linear - often overlapping**
- **NOT business as usual**
  - **risk assessment based on simple extrapolations is risky**

# ACUTE vs CHRONIC TOXICITY ??

- **Acute vs Chronic exposure - duration**
- **Acute vs Chronic response**
  - **delay**
  - **severity**
  - **frequency factor**
- **Propensity of lung for all permutations of exposure response relationship**


B
A
RISK ASSESSMENT
RESPONSE
EXPOSURE

# BOTTOM LINE OF ALL THIS COMPLEXITY

- Response "Cliff" over which you dont want to go
- Finding that Cliff requires looking for it specifically
- Risk assessment
  - risky to freely manipulate concentration x time product
  - appropriate endpoint(s) and animal model(s)

# PROCESSES IMPACTED BY THESE FACTORS

- Engineering decision process
  - choice of agent(s)
  - choice of delivery method
  - cost effectiveness - early testing
- Risk assessment issues
  - regulatory issues
  - human factors
- Liability

# THE GOOD NEWS

- Aerosol factors can be adjusted
  - non respirable particles
  - non toxic contituents
- Results directed toxicity testing can
  - identify exposure response characteristics
  - minimize risk in Risk Assessment
  - save money & time
- There are solutions

# THE not so GOOD NEWS

- Inhalation toxicity of fire suppressants (particularly aerosols) is:
  - very complex - convoluted
  - not readily predictable
- Historical data are:
  - not amenable to simple extrapolation
  - may be of little use or misleading
- NO simple ("painless") solutions