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INTRODUCTION

BRADFORD HILL CRITERIA

WHAT MAKES A FIBER PATHOGENIC?

There is no intrinsic toxic chemical property of a fiber. It is the physical-chemical nature. The 3 Ds plus one.

- **Dose – The primary determinant of pathogenicity.**
- **Dimension – Must be respirable.**
- **Durability (Biopersistence) – The fiber must be able to reside in the lung for long periods of time.**
- **Surface activity – Initiates a cascade of pathogenic events.**

PERTINENT ANIMAL STUDIES

- **An abundant number of animal studies using various methods of exposure clearly show that asbestiform types of various minerals incite fibrosis, lung cancer and mesothelioma in rodents.**
- **Many of the same studies and similar ones show that cleavage fragments do not cause either lung cancer or mesothelioma in rodents.**

PERTINENT IN VITRO STUDIES

- **An abundant data base shows that asbestiform and cleavage fragments of the same mineral have distinctly different activities in various cell systems.**

BRADFORD HILL CRITERIA

Developed for epidemiology studies, but are applicable to toxicology.

1. **Strength of the association.**
2. **Consistency**
3. **Specificity**
4. **Temporality**

BRADFORD HILL CRITERIA

5. **Biological gradient**
6. **Plausibility**
7. **Coherence**
8. **Experiment**
9. **Analogy**

SUMMARY

- **The weight-of-the-evidence using the Bradford Hill paradigm strongly suggests the pathogenic potential of cleavage fragments is clearly less than that of the asbestiform variety of the same mineral.**
- **There is no evidence that cleavage fragments are carcinogenic in rodents but their asbestiform counterparts clearly are.**
- **Roadmap**