Perspectives from the National Academy of Science: The Importance of Background

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SCIENCE AND DECISIONS: ADVANCING RISK ASSESSMENT

National Research Council
Committee on Improving Risk Analysis Approaches Used by EPA
Board on Environmental Studies and Toxicology

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Factors that Contribute to Risk

Community Factors

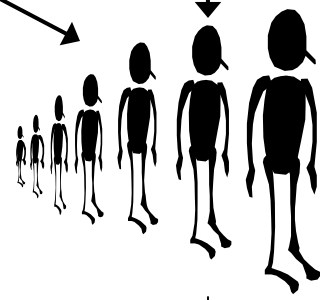
Housing
Medical Care
Education

Host Factors

Genetics, Age
Lifestyle, Disease

Chemical Exp

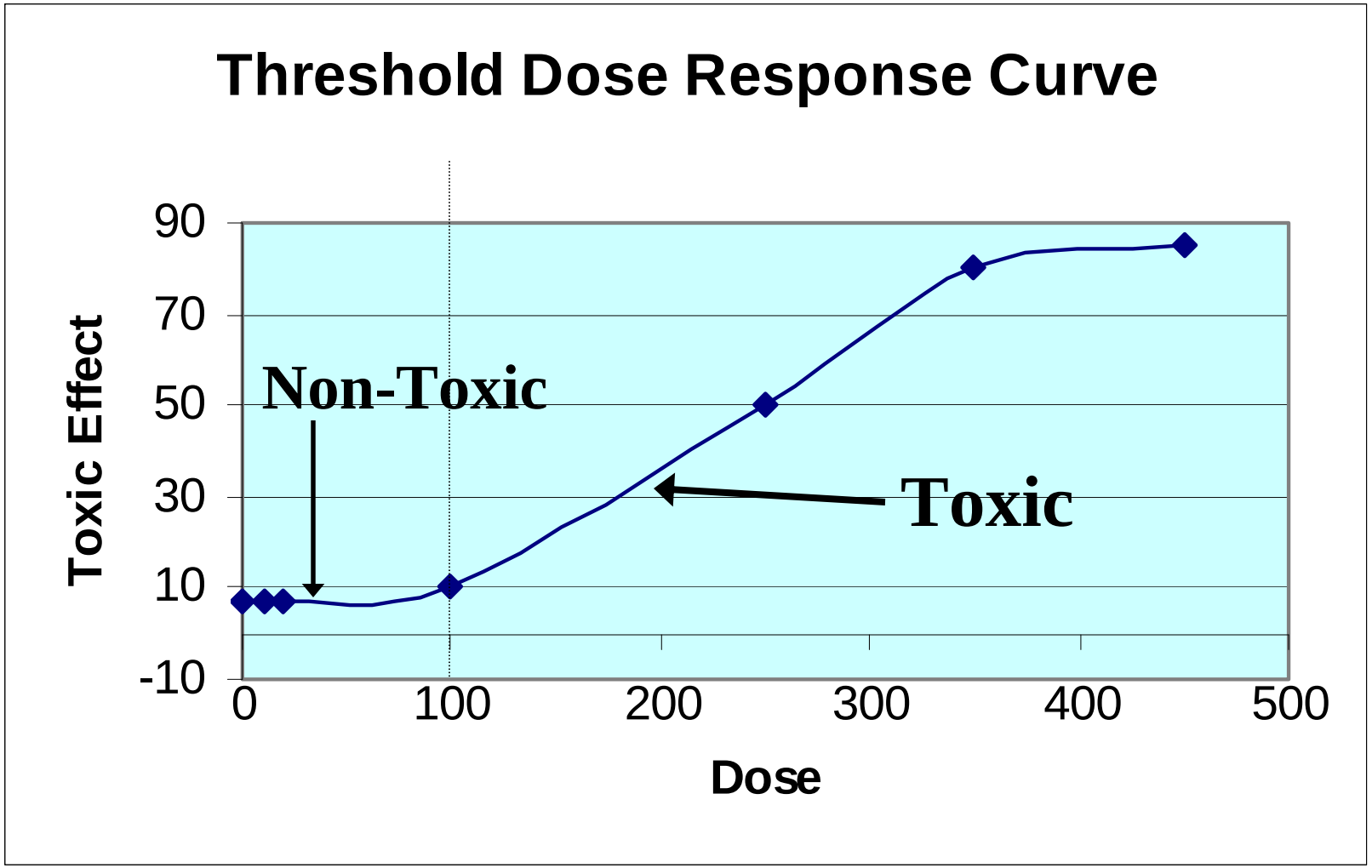
Air, water, soil,
consumer prod, food

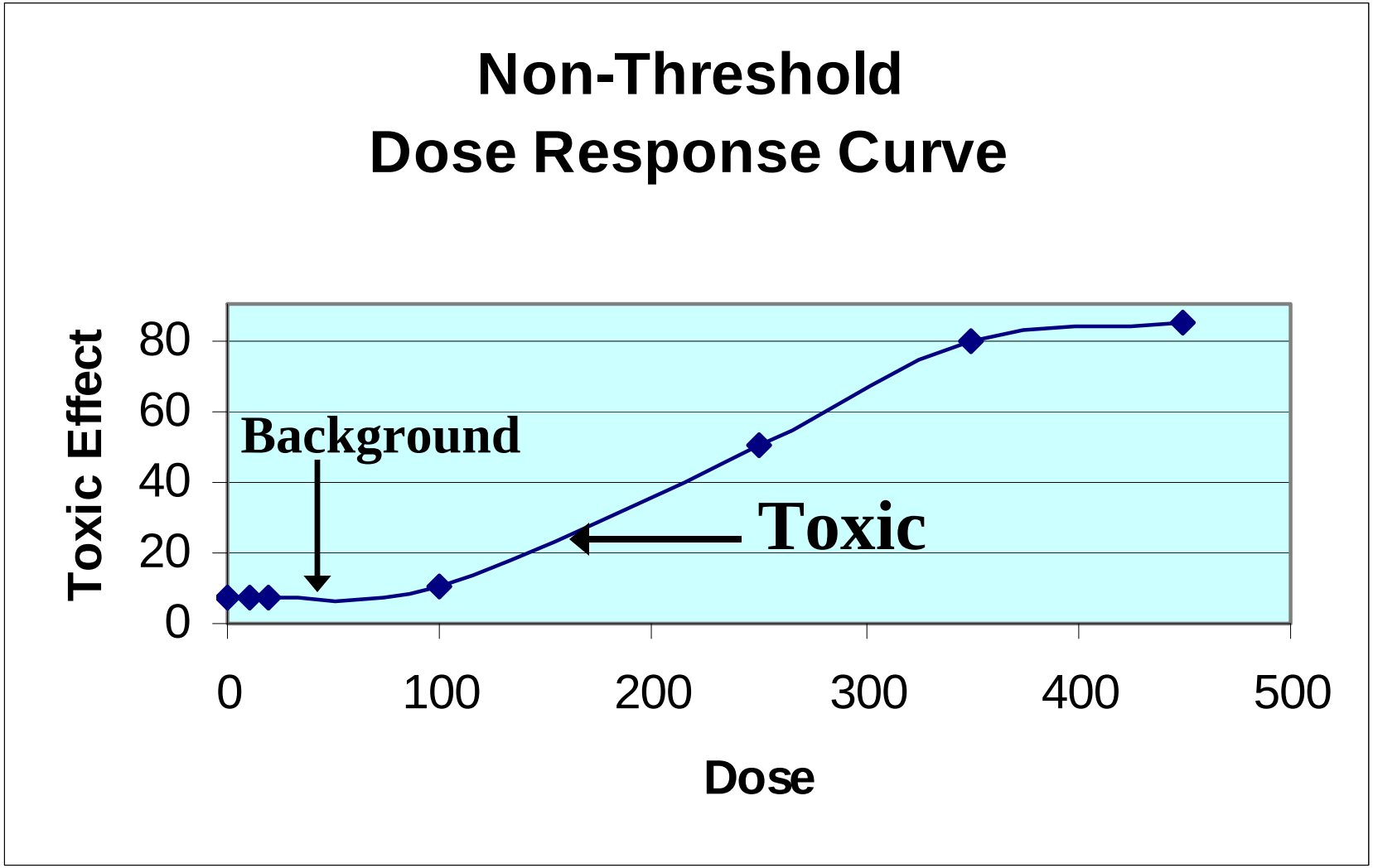


Disease??

- Background exposures and underlying disease processes contribute to population background risk

→ can lead to linearity at the population doses of concern


Threshold Dose Response Curve
Toxic Effect
90
70
50
30
10
-10
Non-Toxic
Toxic
0
100
200
300
400
500
Dose


Non-Threshold
Dose Response Curve
Toxic Effect
80
60
40
20
0
Background
Toxic
0
100
200
300
400
500
Dose

Additivity to Background Aging, Disease or Vulnerability

- Chemical by itself: kidney damage in 200 out of 1000 workers at 100 ppm in air
- Chemical itself: no damage below 1 ppm
- However, backgrnd incidence = 10%
  - 100 workers at high risk – chemical increasing their odds of getting renal disease
- If backgrnd incidence were zero – there may not be any increase in risk at low dose

Its All About Background

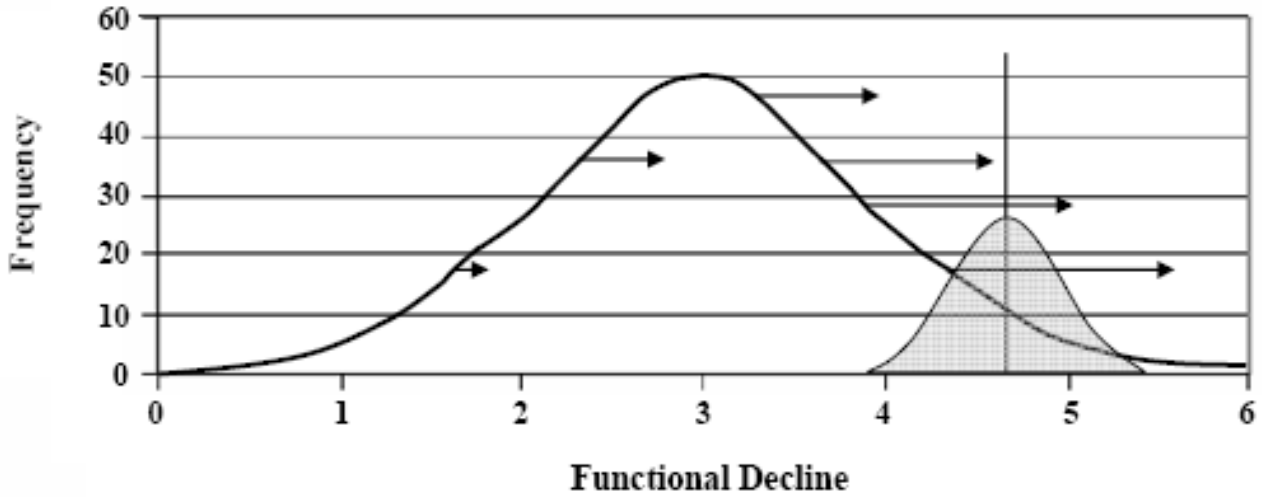


FIGURE 5-9 Population vulnerability distribution. Arrows represent hypothetical response to same toxicant dose for people at given level of functional decline unrelated to any particular toxicant. Vertical line represents presumed threshold between overt adverse and nonadverse effect in median person. Shaded area straddling line represents distribution of thresholds in population.

Background Created by

- Exposures to similarly acting chemicals
  - Add chemical exposures – together they may surpass a threshold
- Ongoing aging and disease processes
  - Decreased functional reserve
  - Decreased defenses
  - Degenerative processes are a toxic response
    - Lipid peroxidation, inflammation, cell death

Background Contribution is Source of Variability

- Risk assessment approaches to variability
  - Cancer - avg person
  - Non-cancer –10 fold more sensitive than avg
    - Still a bright line that's safe for everyone
- New thinking – everyone has a different threshold
  - Population level – no threshold – low doses may cause risk if there is additivity to backgrnd

Examples of Background Addition

- Particulate Matter and background of cardiopulmonary disease
- Ozone and airway hyperreactivity
- 1,4-Dioxane and pre-cirrhotic liver inflammation
- TCE and autoimmune dx –
  - Lupus mouse model
- Mercury and atherosclerosis

Other Sources of Variability

- Childhood (pre- and post-natal)
  - Intake rate, metabolism, clearance, windows of vulnerability
- Nutrition, life style, stress level
- Genetic variation
  - Metabolism
  - DNA repair
  - Host defenses

Research Challenges

- Understand how chemicals interact with aging, disease and susceptibility factors
- Understand how chemicals interact – more than just adding risk, but shifting threshold
- Incorporate this into RA to better protect vulnerable populations
- Keep in mind that current methods may not protect everyone
- Interim default approaches that are reasonably protective & set the stage for more refined models

Colleagues

- Chapter 5 Committee
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- Children's Issues
  - **Melanie Marty**
- USEPA
  - **Bob Sonawane, Kate Guyton**
  - **Brenda Foos, Michael Firestone**
- Clark University
  - **Dale Hattis**