

# Visual and Ocular Effects

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## Level of Evidence Conclusions

- **Animal Studies**

- Initial time period (>24 hours to 7 days): Inadequate level of evidence
- Intermediate time period (8 days to 1 year): Inadequate level of evidence
- Extended time period (>1 year): Inadequate level of evidence

- **Human Studies**

- Initial time period (>24 hours to 7 days): Moderate level of evidence
- Intermediate time period (8 days to 1 year): Moderate level of evidence
- Extended time period (>1 year): Inadequate level of evidence



## Animal Data

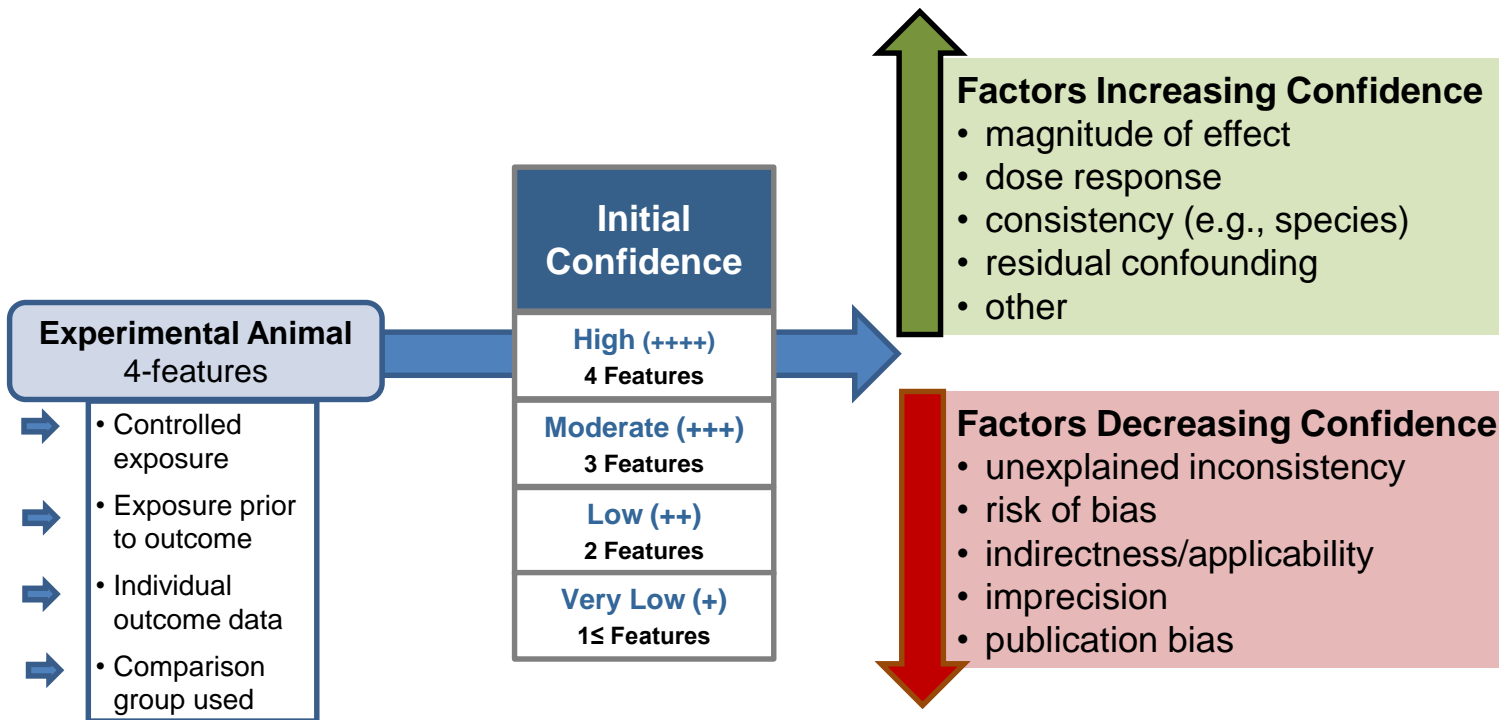
- Bodies of evidence
  - **Initial time period:** 3 studies
  - **Intermediate time period:** 1 study
  - **Extended time period:** 1 study
- Effects:
  - **Initial:** No or inconsistent effects reported
    - No effects on pupil diameter in rats at 1–7 days in 2 studies
    - Increased pupil diameter in rats at 1–7 days in 1 study (Mioduszewski 2002)  
(pattern of effect does not correspond to human data and not clear if it is adverse or reflects recovery)
  - **Intermediate and Extended:** No effects observed
    - No effects on visual functional observational battery scores in 1 study (Kassa 2001)  
3–12 months after acute sarin exposure



# Confidence Considerations to Support Level of Evidence

## Animal – Visual and Ocular Effects

- **Initial time period:** 3 experimental animal studies
- **Intermediate and Extended time periods:** 1 experimental animal study





# Confidence Considerations to Support Level of Evidence

## Animal – Visual and Ocular Effects

- Factors that decreased confidence

**Initial**


- Unexplained Inconsistency ↓
  - Inconsistent results (no effect and increase)


**Intermediate  
and  
Extended**

- Unexplained Inconsistency ↓
  - No ability to evaluate consistency – single study
- Risk of Bias ↓↓
  - Probably high for all 3 key questions (randomization, exposure characterization, and outcome assessment)

- Factors that increased confidence

- No changes for any factors for all 3 time periods

- 
- unexplained inconsistency
  - risk of bias
  - indirectness/applicability
  - imprecision
  - publication bias

- 
- magnitude of effect
  - dose response
  - consistency (e.g., species)
  - residual confounding
  - other



# Visual and Ocular Effects

## Visual and Ocular Evidence Profile for Sarin

INITIAL CONFIDENCE for each body of evidence (# of studies)	Factors decreasing confidence “---” if no concern; “↓” if serious concern to downgrade confidence					Factors increasing confidence “---” if not present; “↑” if sufficient to upgrade confidence				FINAL CONFIDENCE RATING
	Risk of Bias	Unexplained Inconsistency	Indirectness	Imprecision	Publication Bias	Large Magnitude	Dose Response	Residual Confounding	Consistency Species/Model	
<i>Animal</i>										
<b>Initial period - Initial High</b> (3 mammal studies)	---	↓	---	---	---	---	---	---	---	Moderate
<b>Intermediate period – Initial High</b> (1 mammal study)	↓↓	↓	---	---	---	---	---	---	---	Very Low
<b>Extended period – Initial High</b> (1 mammal study)	↓↓	↓	---	---	---	---	---	---	---	Very Low

- No or inconsistent visual or ocular effects reported > 24 hours following acute sarin exposure
- Overall, **Inadequate to evaluate potential sarin-related effects** at all time periods based on the limited number of studies, risk-of-bias concerns, and no evidence of an effect that corresponds with the human data



## Human Data

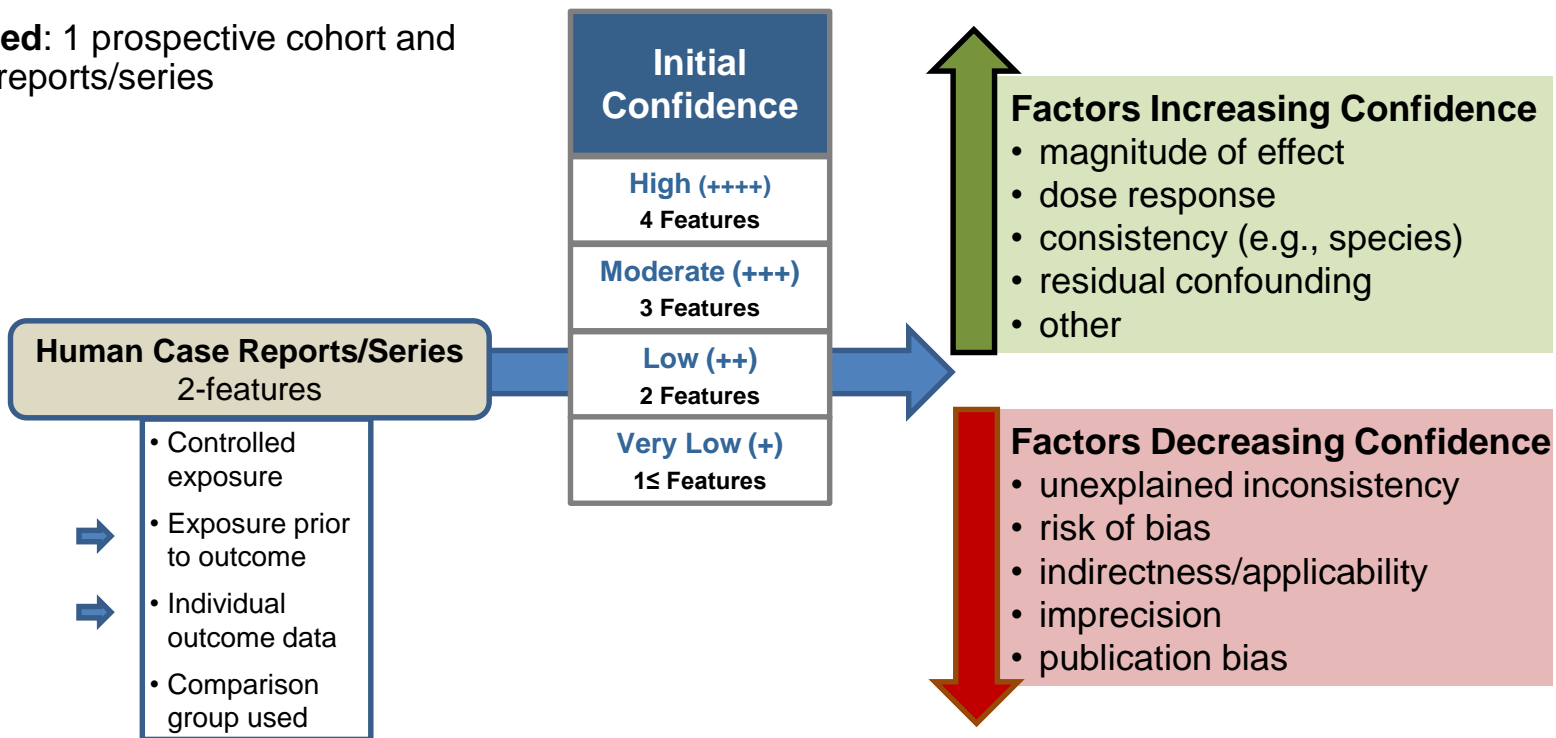
- Bodies of evidence
  - **Initial time period:** 5 case reports/series
  - **Intermediate time period:** 2 cross-sectional studies; 8 case reports/series
  - **Extended time period:** 1 prospective cohort study; 4 case reports/series
- Effects
  - **Initial:** Consistent evidence for pupil constriction (miosis) and evidence of other symptoms (e.g., blurred vision, ocular pain, difficulty focusing) 1–7 days following exposure
  - **Intermediate:** Consistent evidence for pupil constriction for weeks, suggests persistence following exposure; Then, pupil constriction not found at 1-2 months, suggests recovery
    - Slower visual evoked potentials (VEPs) reported at 6-8 months
    - Other symptoms reported in small percentages of subjects for months
  - **Extended:** Some evidence of symptoms in small percentage of study subjects 1–5 years following exposure



# Confidence Considerations to Support Level of Evidence

## Confidence Conclusions Primarily Based on:

- **Initial:** 5 case reports/series
- **Intermediate:** 2 cross-sectional studies
- **Extended:** 1 prospective cohort and 4 case reports/series



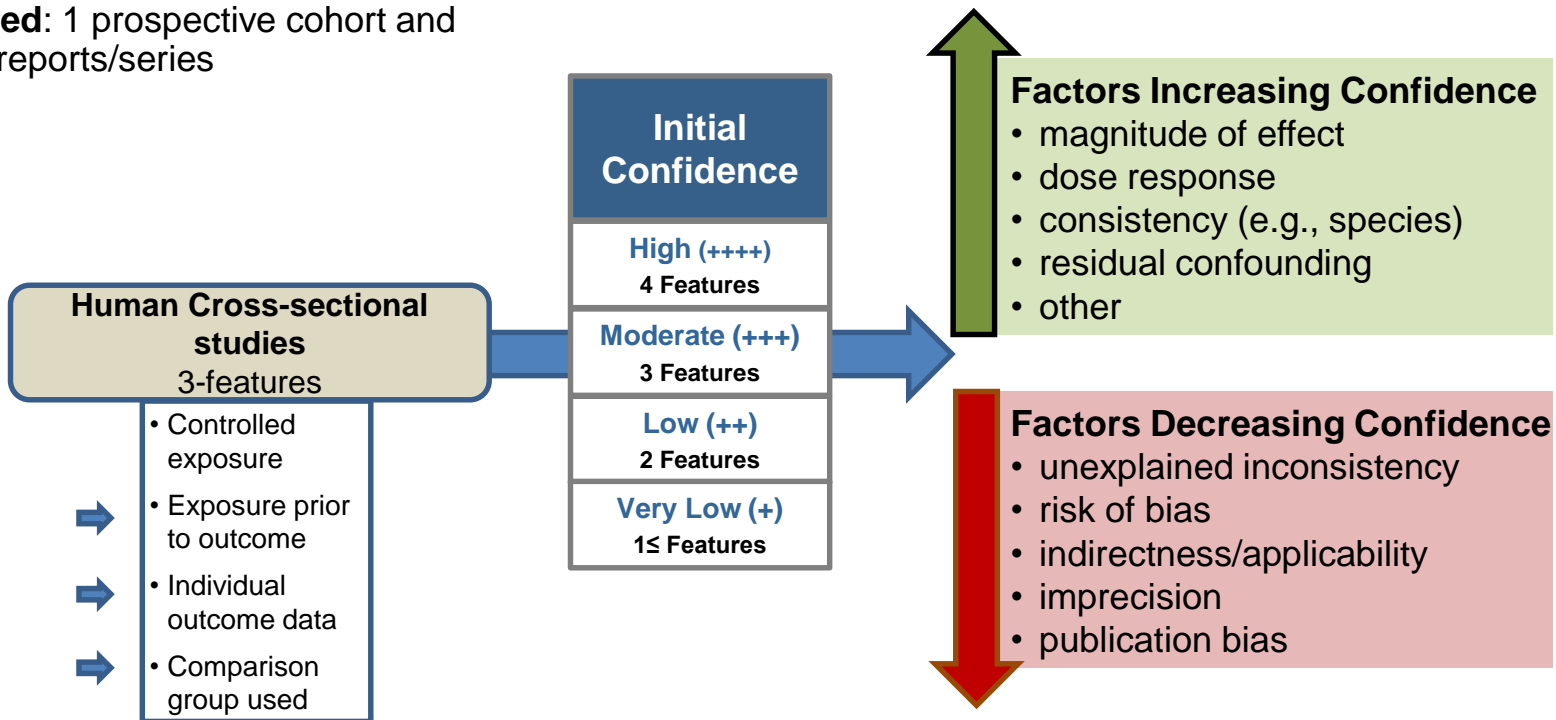




# Confidence Considerations to Support Level of Evidence

## Confidence Conclusions Primarily Based on:

- **Initial:** 5 case reports/series
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# Confidence Considerations to Support Level of Evidence

## Human – Visual and Ocular Effects

- Factors that decreased confidence

Intermediate and Extended

- Risk of Bias (case reports/series) ↓
  - Probably high for 2 key questions in most studies (confounding and blinding of outcome assessors)

Extended


- Risk of Bias (single prospective cohort) ↓↓
  - Probably high or definitely high for 2 key questions and other serious risk-of-bias concerns


- Factors that increased confidence

Initial

- Magnitude of Effect (upgrade considered\*)
- Consistency ↑

\* *Decision to upgrade once based on magnitude of effect and consistency collectively, and supported by well-established response of immediate constriction of the pupils in the first 24 hours following acute sarin exposure*

- 
- unexplained inconsistency
  - risk of bias
  - indirectness/applicability
  - imprecision
  - publication bias

- 
- magnitude of effect
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<i>Human</i>										
<b>Initial period – Initial Low</b> (5 case reports/series)	---	---	---	---	---	---	---	---	↑	Moderate
<b>Intermediate period - Initial Moderate</b> (2 cross-sectional studies)	---	---	---	---	---	---	---	---	---	Moderate
<b>Intermediate period – Initial Low</b> (8 case reports/series)	↓	---	---	---	---	---	---	---	---	Very Low
<b>Extended period – Initial Moderate</b> (1 prospective cohort study)	↓↓	---	---	---	---	---	---	---	---	Very Low
<b>Extended period – Initial Low</b> (4 case reports/series)	↓	---	---	---	---	---	---	---	---	Very Low

- **Moderate confidence** that acute sarin exposure is associated with visual or ocular effects from days to months following exposure
- **Limitations:** Risk-of-bias concerns, uncertainties related to study design for the case reports/series



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Questions?