### Miller 1979 USA Hospital Multicenter Prospective cohort 1966 to 1975
#### Study
- **Purpose:** To provide quantitative date on the effects of chloral hydrate in hospitalized medical patients monitored by the BCDSP.
- **Inclusion:** Consecutive admissions Use of chloral hydrate therapy
- **Exclusion:** Not described

#### Population
- **N = 26,294 n = 5435 (21%) received chloral hydrate**
- Men and women (40%) Mean age 57
- Cardiovascular disease most common primary diagnosis
- 10% died during hospitalization

#### Intervention
- Trained monitors (nurses or pharmacists) use self-coding forms to record information
  - Patient characteristics
  - Diagnosis (es)
  - Drugs prescribed
  - Dose (details)
  - Duration of therapy
- Physician interview to determine indication
- Determination of satisfactory/unsatisfactory/don’t know efficacy obtained from physician upon discontinuation of drug therapy
- AEs observed
- Physician determination of whether AE related to drug/dose
- Independent second opinion by clinical pharmacist

#### Results
- **Reported indication for chloral hydrate therapy**
  - 97% insomnia
  - 0.5 gm = 81%
  - >3 days = 37%
- **Usual dose**
  - Benzodiazepines = 21%
    - Diazepam
    - Chlordiazepoxide
- **Duration**
  - Overall = 15%
  - 14%
  - 16%
  - Failure rates declined with increasing age, were slightly lower in male patients and in those who received concurrent benzodiazepines
- **Most common other drugs prescribed**
  - Norine = 15%
  - 14%
  - 16%
- **Adverse reactions**
  - CNS depression
    - 2.2% (overall)
    - 1.1% (daytime drowsiness most common)
    - <1%
  - GI disturbance
  - CNS excitation
    - n = 3
  - Life threatening
  - Factors influencing adverse reactions
    - More common with
      - 1.0 gm dose
      - Age >50
      - Higher frequency of CNS excitation
      - Patients who died during hospitalization
      - Concurrent therapy with benzodiazepine
      - Elevated blood urea nitrogen

### Comments
- There was no evidence of adverse cardiac associated with chloral hydrate, which have been observed in some cases of overdosage.
- There was a significant difference between the 0.5 and 1.0 gm doses for patients who failed to sleep well, suggesting that a dose between 1.5 and 2.0 gm is needed for an adequate hypnotic effect.
- There is little rationale for administration of chloral hydrate at bedtime concurrently with daytime use of a long-acting benzodiazepine.

### Conclusion
Adverse reactions to chloral hydrate in the hospital setting are uncommon, occurring in about 2% of recipients. CNS depression is the most common type of adverse reaction, and it appears to become more frequent with increasing dosage inpatients older than 50 years, who died during hospitalization, in patients who received a concurrent benzodiazepine, and in patients with elevated blood urea nitrogen levels.