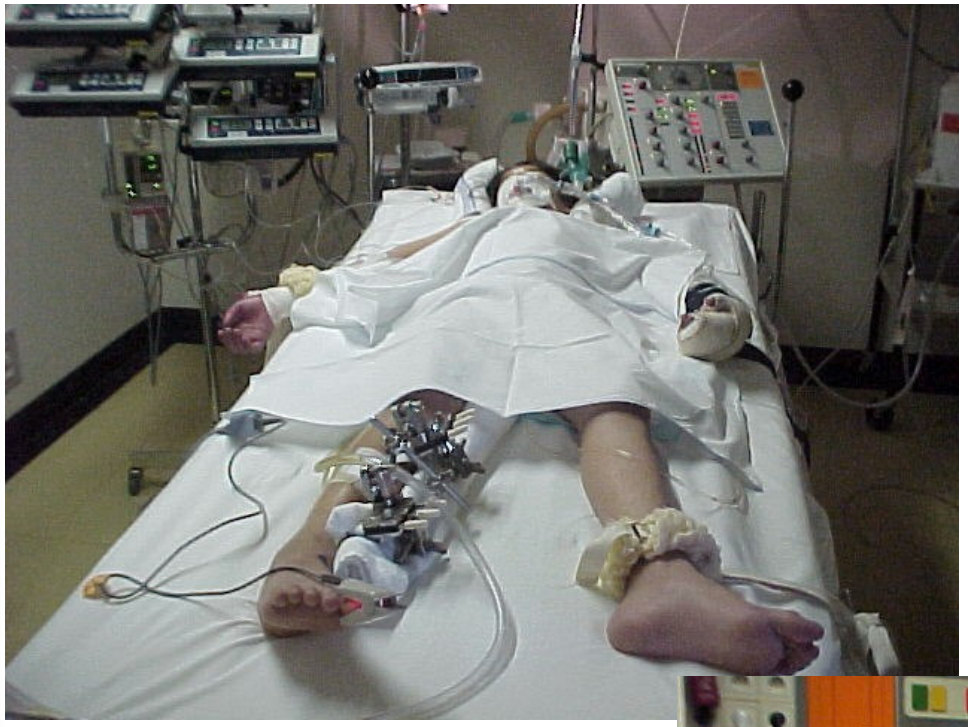
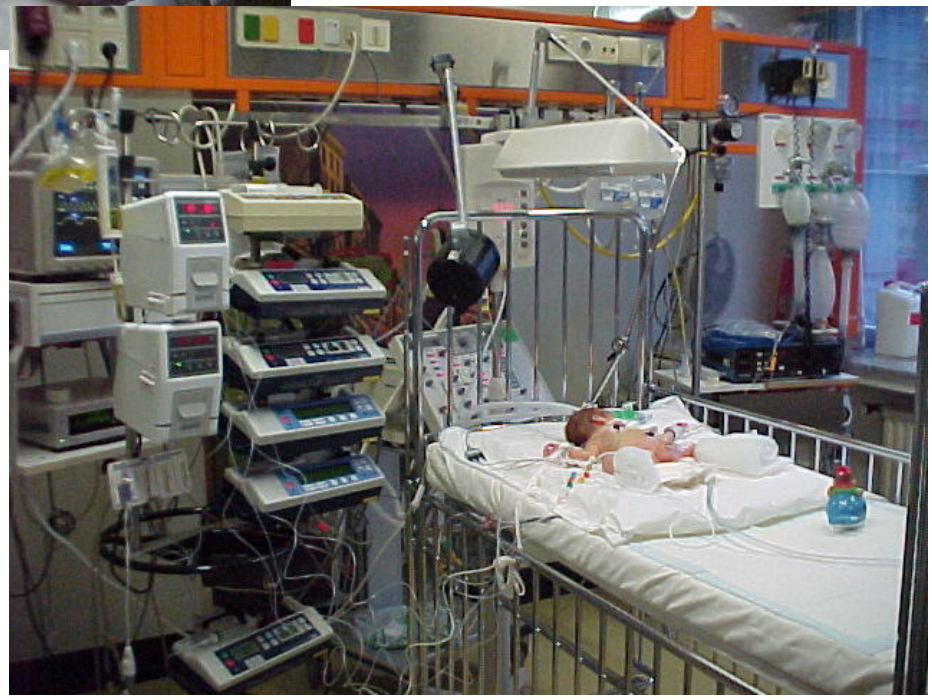
MEDICINES FOR CHILDREN
the CESP perspective

José Ramet MD PhD





Analgesia

Sedation

Antibiotics

Paralyzing drugs

Gastric protection

...

European pediatric hospitals

			Off-label	Unlicensed
Conroy	1998	Gen ped Hosp	39%	7%
Turner	1996	PICU	23%	14%
Conroy	1999	NICU	55%	10%

Consequences of unlicensed and off-label use of medicines in children

- **Quality:**
  - absorption characteristics and bioavailability unknown
  - most likely risk :

    inaccurate dosing inefficiency

- **Safety** : unknown adverse effects

- **Efficacy:**
  - new major therapeutic breakthroughs : not available for children
    - treated with older - less efficacious - products
    - new medicines used without appropriate studies
      - not same efficacy as in adults / effect not similar
      - increase morbidity and mortality of children

Child... Not a small adult

Infant... Not a small child

Preterm... Not a small infant

- Studies in adults not sufficient
  - Specificity disease
  - Kinetic characteristics
  - Effects on growth, development, maturation
  - Specific adverse reactions
- Additional problems
    - Incapable give legal consent
    - Medicines if clinical value
    - Best possible protection
    - Minimization risk and pain

initiatives on paediatric medicinal products?

- **1. Increase the availability** medicinal products
  suitably adapted to the needs of children by encouraging :
  - appropriate pediatric studies on new medicinal products
  - studies on existing products
  - development of suitably adapted formulations

- **2. Ensuring that pharmacovigilance mechanisms are adapted**
  - Possible long-term effects in specific cases

- **3. Avoiding unnecessary studies**
  - Publication of details of clinical trials already initiated

- **4. List of priorities for research**
  - on existing medicinal products
  - in accordance with health needs
  - priorities in different therapeutic classes

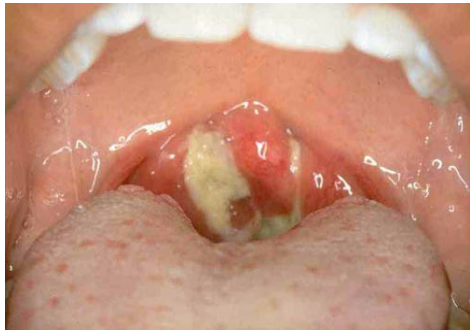
- **5. Expert group**
  - in the field of research
  - development and assessment of clinical trials

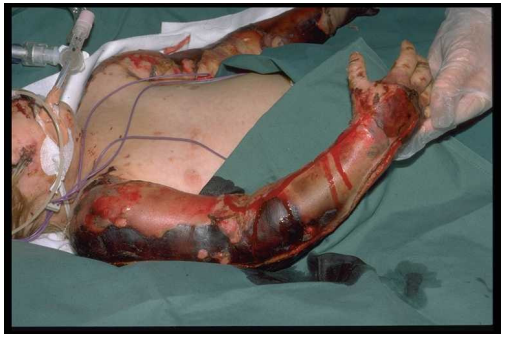
- **6. Highest ethical criteria**

Avenues to explore

- Positive Incentives for research
- specific rules to encourage the performance of clinical trials in children
- Legal EU requirements
- Transparency and central database
- Scientific expert group
- European network of clinical excellence

Future ?





"It is difficult to make predictions

... especially about the future"

Y. Berra

C.E.S.P.

Current situation

- European Union
  - 0-16 years : about 75 million people

- 0-16 years group : specific sub-populations
  - Age groups: different developmental and behavioural characteristics
  - Age-specific needs

Empiricism

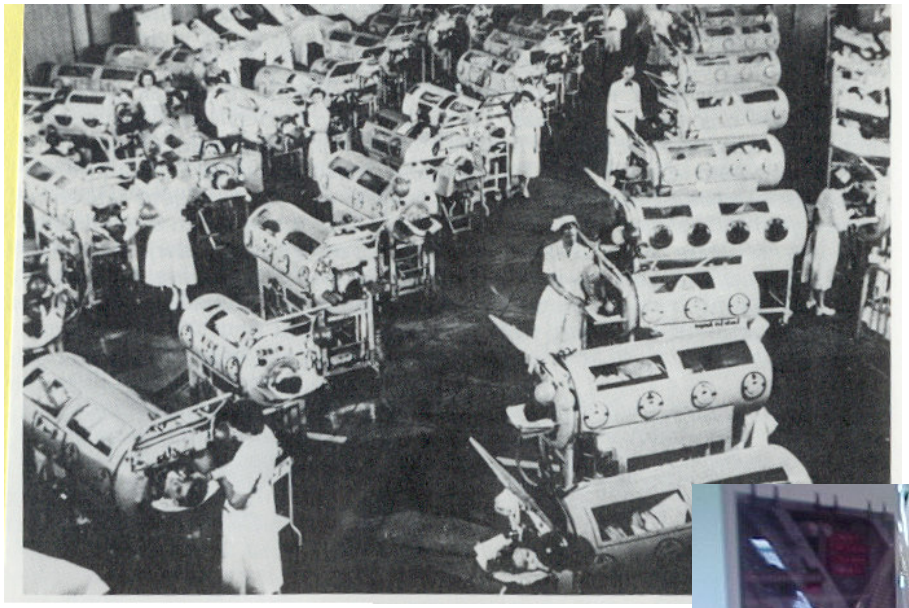
- Empiricism : wrong?
- No, but

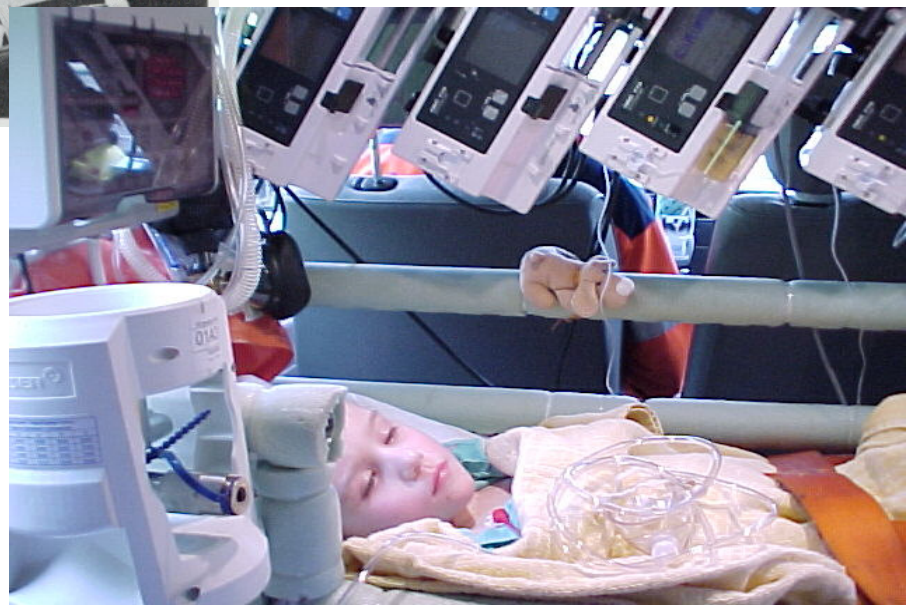
  Difficult to accept

  If strong evidence missing: rely on ... absence of data

  - Uncontrolled studies
  - Case reports / anecdotical reports
  - Not published information
  - Meta-analysis
    - Negative studies not published
    - Homogeinity bias
    - Size
    - Blinding

How did we work until now?





Introduction

Treated with a medicine

ADULT

- sure : extensively tested
- to assure
  - safe
  - effective
  - high quality for use

CHILD

- may not be true
- over 50% of those used
  particularly in specialized medicine
- Potential risk
  - lack of efficacy
  - unexpected adverse effects
  - even death

Historical background

- drug catastrophes involving mainly children
  - sulphanilamide 1937
  - thalidomide 1962

- development of regulations concerning medicinal products

- stringent criteria of (pharmaceutical)
  - quality
  - safety
  - efficacy

unfortunate paradox :children benefited the least

→ “Therapeutic orphans”

H. Shirkey 1963 :reflect problems re. regulatory requirements

How did we work until now?

Indications... without research

- Promising case report published
- Uncontrolled study suggests benefit
- Use: standard for many years