Bronchial provocation testing

ICOH
Mexico 2012

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Outline

• definitions, concepts and some history
• indications
• methods
• difficulties
• summary: should every department do it?

• note: workplace challenge tests not covered
Definitions and concepts

Synonyms:
- bronchial provocation testing
- specific provocation testing
- specific inhalation testing
- specific inhalation challenge (SIC) - preferred

The observation of responses to a controlled exposure to an **occupational** agent, in the investigation of:

- occupational asthma (>95%)
- occupational alveolitis (HP)
A little history

SIC was devised by Jack Pepys in a corridor of the Brompton Hospital in London in the 1960s. Early test agents included:

• diisocyanates
• detergent enzymes
• colophony
• moulds

Anxieties over the fire risk of SIC with diisocyanates/solvents persuaded the hospital to build a set of dedicated challenge ‘chambers’ with large observation windows, sealed doors and a local exhaust system; destroyed when the hospital sold its building to a property developer.

The first publication to describe the technique for asthma was a description of the detergent enzyme ‘outbreak’ at Lever Bros.

A little more history

Remarkably little development since, except:

‘dosimetry’

- the use of machine-delivered and titrated doses of test agent
- Jean-Luc Malo at Sacré Couer Hospital (Montreal

“Because the realistic approach can lead to erratic exposures if the administered concentration or dose of the agent is not carefully controlled, with the threat of considerable and immediate asthmatic reactions, closed-circuit apparatuses have been proposed.”
Indications

Broadly these are of two kinds:

1. a diagnostic requirement: ‘jurisdictional’
   
some compensation schemes require that the diagnosis of OA is made using SIC, notably
   • Quebec
   • Finland

2. a diagnostic adjunct: more commonly
   
   • when other, simper methods have failed to secure (or exclude) a diagnosis
   • when a novel agent is being considered
   • when it is important to distinguish one agent from another in mixed exposures

3. (medico-legal: generally frowned upon and rarely, if ever, done)

NB:
the very different test populations in the above make it difficult to transfer experience across:
- a source of considerable misunderstanding
Methods

1. Delivery of test agent

   - ‘realistic’ or ‘Pepys’ method: most units use this approach
     The attempted recreation of exposure conditions at work
     Protocol-driven ± exposure-measurement starting at low doses
     - ‘dust-tipping’ (flour, enzymes)
     - spray painting (HDI)
     - soldering (colophony)
     - sanding (wood dusts)
     - painting (liquids)
     - glueing
     - etc
     ‘appropriate’ exposure, but can be difficult to control dose

   - ‘dosimetry’: Montreal, Helsinki
     controlled exposures
     but not possible for all agents and technical problems++
     expensive (capital and maintenance)
Methods: ‘Pepys’

- Spray painting
- Soldering
- Dust-tipping (flour)
- Sanding (wood dust)
- Heat-sealing (bakery worker)
Methods

2. Selection and preparation of patient

- ‘sufficient’ baseline lung function
  - *eg* FEV1>1.5L

- normal asthma treatments: two approaches
  - stop all except *prn* salbutamol
    - increased confidence in negative SIC result
    - possibly reduces likelihood of false negative SIC, but
    - may render asthma unstable and make SIC impossible (unusual)

  - continue prophylactic medicines but at low dose (*eg* evenings only)
    - ensures greater stability of underlying disease, but
    - may make it difficult to interpret negative SIC result

- inpatient/outpatient: variable practice but prolonged observation is mandatory

- informed consent = good governance
Methods

3. Test protocol: principles

- ‘controlled’: comparison with response to similar, but inert, agent
- single-blind:
  - sometimes double-blind
  - sometimes impossible (e.g., sanding wood)
- separate agents on separate days
  - safety
  - assessment of late responses
- repeat tests
  - valuable to confirm positive responses
  - dose-response may be useful validation
  - reduces likelihood of false negative interpretation
stop all asthma treatment (except SABA) for 10 days

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<th>am2</th>
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<td>admit to hospital: spirometry training, consent</td>
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<td>day 2</td>
<td>baseline FEV1 histamine pc20</td>
<td>SIC (inert)</td>
<td>regular spirometry</td>
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<td>SIC (inert/active)</td>
<td>regular spirometry</td>
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etc as required
4. Measuring responses

- reproduction of work-related symptoms

- spirometry (FEV\textsubscript{1})
  - repeatedly
  - frequently in first hour,
  - hourly thereafter

- NSBHR
  - before/after SIC series (or more frequently)
  - helps to distinguish ‘immunological’ form ‘irritant’ responses

- other measures (under investigation)
  - induced sputum
  - FeNO
5. Assessing responses

• What makes a positive test?

  • reproducible reproduction of work symptoms on active (but not control) exposure
  • reproducible asthmatic response via \( \text{FEV}_1 \) on active (but not control) exposure
    • consistent fall >15% (‘traditional’)
    • early vs prolonged vs late vs dual
  • increase in NSBHR (>doubling dose)

  • (?) ditto *re* sputum eosinophilia/FeNO

• = ‘full house’
• more usually, some element of judgement
Downsides and pitfalls

• expensive and time-consuming

• false negatives (despite ‘gold standard’ reputation)

• hazardous
  • but risk is low in experienced hands
  • starting doses low, and
  • based on severity of patient’s symptoms at work
  • careful observation through to late response
  • access to resuscitation
Should you be doing this?

Few centres do
• except those that ‘have to’
• ~20 worldwide
• almost all in Europe
• (none in US)

Capital investment is high
• challenge chamber(s)

Staffing requirements high
• nursing/technical/medical time

Perhaps only necessary in single national/regional centre

(note: ERS Taskforce on SIC to report in 2013
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