

# Aridol

## Bronchial challenge testing with inhaled dry powder mannitol

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The logo for BTC health, featuring the text "BTC health." in a bold, blue, sans-serif font. The logo is positioned on the right side of the slide, partially enclosed by a large, stylized, multi-colored circular graphic that transitions from light blue to green.

# Aridol Challenge

## Overview



*'For identifying bronchial hyperresponsiveness to assist in the diagnosis of asthma'*

# Aridol Challenge

## Overview

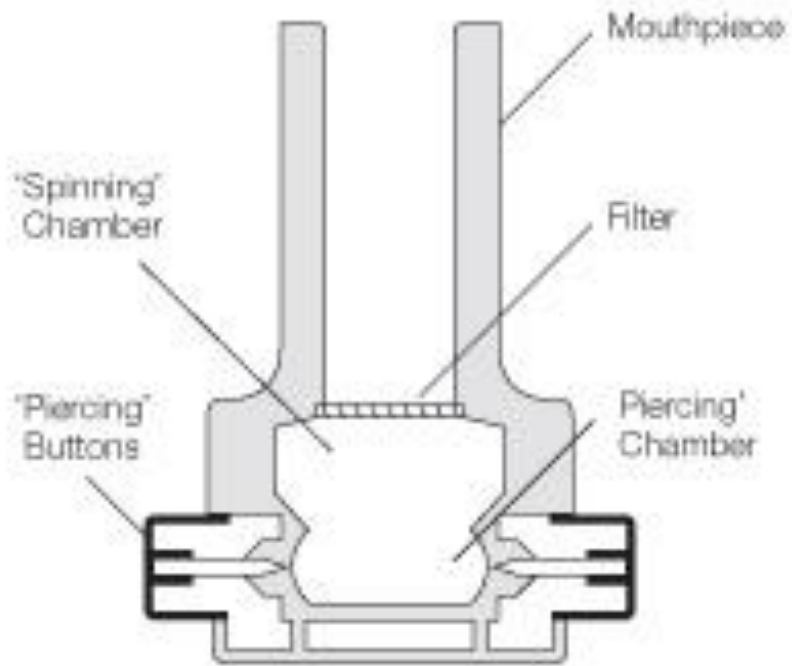
- Standardised (single-use) test kit containing sufficient capsules to complete one maximum dose challenge, and an inhaler
- Minimal preparation, no dilutions or clean up
- Average test time to a negative test less than 30mins
- No nebulizer- minimising impact on asthmatic technicians
- No specialised equipment required (other than spirometer)

## High Specificity

- 95% specificity
- High positive predictive value (98%)
- Can confirm/exclude Asthma in the presence or absence of symptoms

# Aridol Inhaler Device

Aridol™ inhaler device



# Aridol Test Protocol

- Progressive protocol: 0, 5, 10, 20, 40, 80, 160 (3x) mg
- Measurements: FEV<sub>1</sub> post dose
- Positive response: Fall in FEV<sub>1</sub> ≥15% or ≥10% between consecutive doses calculated from 0mg baseline
- Time taken: 17 minutes (mean positive test)  
26 minutes (mean negative test)
- Recovery: Spontaneous recovery to baseline FEV<sub>1</sub> in 30-60 mins (or bronchodilator)

# Aridol Challenge

Prior to testing

- **Withholding medications:** as appropriate + no caffeine, chocolate, smoking, vigorous exercise prior to test
- **Contraindications:** hypersensitivity to mannitol or gelatin or conditions compromised by induced bronchospasm/repeated blowing maneuvers (aortic/cerebral aneurysm, uncontrolled HT, MI CVA in last 6 months)
- **Precautions:** inhaled only (not swallowed), must be undertaken only by trained professional equipped to manage acute bronchospasm, patients should not be left unattended during test.
- **General precautions for spirometry and BCTs:**  $FEV1 \leq 70\%$  predicted or 1.5L in adults, recent ocular surgery, spirometry induced bronchoconstriction, recent RTI, unstable angina, pneumothorax etc.

# Aridol Challenge

## Medication withholding and other restrictions

- There are a number of medications that may decrease bronchial hyperresponsiveness and should be withheld prior to taking an Aridol test
- Ingestion of significant quantities of coffee, tea, cola drinks, chocolate or other food containing caffeine may affect test results (should be withheld on the day of the test (prior to testing))
- Vigorous exercise should not be performed prior to testing on the day of the test
- Smoking: Patients should refrain from smoking for at least 6 hours prior to testing.

Withholding Time	Medication
6 – 8 hours	<b>Inhaled Nonsteroidal Anti-Inflammatory Agents:</b> e.g. sodium cromoglycate (Intal®); nedocromil sodium (Tilade®)
8 hours	<b>Short-Acting Beta 2 Agonists</b> e.g. salbutamol (Ventolin®); terbutaline sulfate (Bricanyl®)
12 hours	<b>Inhaled Corticosteroids</b> e.g. beclomethasone dipropionate (Qvar®); budesonide (Pulmicort®); fluticasone propionate (Flixotide®)  <b>Anticholinergic Bronchodilators</b> e.g. ipratropium bromide (Atrovent®)
24 hours	<b>Inhaled Corticosteroids and Long-Acting Beta 2 Agonist Combination Products</b> e.g. fluticasone and salmeterol (Seretide®); budesonide and eformoterol (Symbicort®)  <b>Long-Acting Beta 2 Agonists</b> e.g. salmeterol xinafoate (Serevent®); eformoterol fumarate (Foradile® or Oxis®)  <b>Phosphodiesterase Inhibitors / Adenosine Receptors</b> e.g. theophylline (Nuelin®)
72 hours	<b>Long Acting Anticholinergics</b> e.g. tiotropium bromide (Spiriva®)  <b>Antihistamines: Over-the-Counter &amp; Prescription</b> e.g. brompheniramine maleate (Dimetapp®); diphenhydramine (Benadryl®); loratadine (Claratyne®); cetirizine (Zyrtec®); fexofenadine (Telfast®); levocetirizine dihydrochloride (Xyzal®)
4 days	<b>Leukotriene-Receptor Antagonists</b> e.g. montelukast sodium (Singulair®)

# Aridol Challenge

Medication withholding and other restrictions

Dose #	Dose mg	Capsules per dose	Cumulative Dose mg
1	0	1	0
2	5	1	5
3	10	1	15
4	20	1	35
5	40	1	75
6	80	2 x 40 mg	155
7	160	4 x 40 mg	315
8	160	4 x 40 mg	475
9	160	4 x 40 mg	635

- A positive response is achieved when the patient experiences either a 15% fall in FEV<sub>1</sub> from baseline (0 mg dose) or 10% incremental fall in FEV<sub>1</sub> between doses



# Aridol Challenge

## Equipment required

- Aridol kit
- Spirometer
- Nose clip (optional)
- Timer (set to 60 seconds)
- Calculator (or spirometer software)
- Bronchodilator
- Oxygen + emergency equipment



# Aridol Challenge

Tips to ensure patient tolerance and to minimise dry powder irritation

- Patient should be seated
- Spirometry training/coaching provided
- Inspiratory flow rate required for device explained/demonstrated
- Glass of water available (for sipping during test if required)
- Maintain a steady inhalation rate (not too fast)
- Tilt head back (to open airway- tell patient to look at ceiling)
- Sip water if necessary



# Other Tips

- Check capsule is empty following each dose
- Only pierce capsule once
- Exhale away from inhaler (to minimise humidity within the device)
- Make sure hands are completely dry (so caps don't get sticky)
- Only remove caps from foil immediately before test/inhalation
- Using tweezers to handle capsules may help minimise static/stickiness
- If you can't hear capsule spin/rattle within device- tap base of inhaler, whilst tilting downwards



# Aridol Challenge

FEV<sub>1</sub> measurements

- Following 60 seconds, have patient perform two repeatable FEV<sub>1</sub> measurements
- Avoid delays between doses to ensure osmotic gradient is maintained
- Stop test when PD<sub>15</sub> reached or when negative test complete

# Performing the Aridol challenge - loading inhaler

## Loading the inhaler



Remove protective cap from inhaler device



Twist open the inhaler in the direction of the arrow on the device



Place capsule in piercing chamber



Pierce capsule by depressing both buttons simultaneously



# Pre-challenge spirometry

Determine baseline

- Standard spirometry
- Assessment of FEV<sub>1</sub> reproducibility
- Establishment of predicted normal value FEV<sub>1</sub>



# Baseline FEV<sub>1</sub> (0mg capsule)

- Inhalation and 5 second breath hold
- 60 seconds timed (from end inhalation)
- 2 x FEV<sub>1</sub> measurements (within 150ml variability or do 3)
- Record **highest** FEV<sub>1</sub> as baseline

# Rest of test

Repeat testing following each dose increment

- Repeat inhalation, 5 second breath hold, and FEV<sub>1</sub> at 60 seconds for all dose steps in the challenge (or until a 10% fall between doses or 15% from baseline is reached)
- For doses using multiple capsules (80mg or 160 mg), perform inhalation, 5 second breath hold, inhalation & 5 second breath hold until the full dose has been inhaled- then perform FEV<sub>1</sub> at 60 second post inhalation of last capsule in the dose
- Minimise delay between doses to maintain osmotic gradient



# End of test

## Monitor recovery

- If a cumulative dose of 635mg has been inhaled without a 15% fall from baseline (0mg) then challenge is considered negative and complete
- Administer post-test bronchodilator as per protocol
- Patients should be monitored until  $FEV_1$  has returned to 5% of pre-challenge baseline



# Aridol challenge

## Outcomes

### Positive Aridol challenge result

- A positive Aridol response may be achieved in 2 ways:
  - $\geq 15\%$  fall in  $FEV_1$  from baseline (using the post 0mg  $FEV_1$  as comparator)
- or
- $\geq 10\%$  incremental fall in  $FEV_1$  (between consecutive Aridol doses)

### Negative Aridol Challenge Result

- An negative Aridol challenge is considered to be :
  - a cumulative dose of 635mg of Aridol has been administered
- and
- $FEV_1$  has not fallen by  $\geq 15\%$  from baseline.

# Aridol challenge

## Summary

- ✓ Strong correlation with active airway inflammation
- ✓ Identifies EIA (exercise induced asthma)
- ✓ Standardised/reproducible
  - Reduction in variability in preparation, delivery with a standardised test kit (ideal for clinical trials)
- ✓ Approved by regulatory authorities
- ✓ Practical benefits;
  - No nebuliser required/ no sterilisation of equipment
  - Good patient acceptability
  - Limits exposure risk for asthmatic technicians performing the test
  - 3 year shelf-life / no wastage

# ARIDOL

## THE GOLD STANDARD IN DIAGNOSIS OF ASTHMA

