CHAPTER 7 – Bronchial Challenge Testing

7.1 Introduction

Controlled challenging of the airways has long been recognised as a laboratory test for assessing airways hyperresponsiveness (AHR). During the test the patient's airways are exposed to a stimulus, which can cause bronchoconstriction in susceptible subjects, those that are hyperresponsive. The amount of bronchoconstriction can then be measured by comparing pulmonary function tests of airways caliber pre and post exposure to the stimulus. Hyperresponsiveness can therefore, be defined as an exaggerated response to the bronchoconstrictor [1]. This mimics the spontaneous variability in airways obstruction as observed in patients with asthma and to a lesser extent in chronic obstructive pulmonary disease (COPD)[2].

AHR is present in almost all patients with asthma when they are symptomatic. Hence, AHR is more pronounced for example after allergen exposure [3]. Variable airflow limitation is recognized as a hallmark of asthma.

When there is persistent inflammation and AHR within the airways in the absence of symptoms and changes in airways caliber this is referred to as the "asthmatic state". The World Health Organisation (WHO) combined working group in 1995 described asthma as "A chronic inflammatory disorder of the airways in which many cells play a role including mast cells and eosinophils; in susceptible individuals this causes recurrent episodes of wheezing, breathlessness, chest tightness and cough, particularly at night or early in the morning. These symptoms are usually associated with widespread but variable airflow limitation reversible either

spontaneously or with treatment and an associated increase in airways responsiveness to a variety of stimuli.

Originally it was thought that challenge testing would separate non-asthmatics from asthmatic subjects but unfortunately non-asthmatic subjects demonstrate a large range of bronchial reactivity ranging from normal to the asthmatic end of the spectrum. Bronchial hyperresponsiveness is not unique to asthma and has been demonstrated in a range of other inflammatory disorders including COPD and allergic rhinitis, i.e. of limited clinical use.

Challenge testing may be used to look for a) specific bronchial hyperresponsiveness: this is when it needs to be established if a subject has been sensitised to a specific substance i.e. a chemical or protein that the subject is working with, or b) non-specific bronchial hyperresponsiveness: this is when we want to establish if the subject's airways are hypersensitive and hyperreactive, 'twitchy', when given low doses of bronchoconstrictor agents.

7.2 Definition of Terms and Units: Principal of Measurement

In bronchial challenge testing we try to reproduce similar conditions to those, which may cause bronchoconstriction in susceptible subjects so the presence and the severity of the ensuing airways obstruction can be assessed. Therefore, the obvious choice of agent to use in provocation testing would be the substance we suspected was causing the bronchoconstriction in the subject. Unfortunately, testing to allergens and occupational sensitisers is not without risk both to the subject and the staff if not undertaken correctly. This is because the tests are not as well standardised as specific pharmacological agents, exercise, cold/dry air hyperventilation challenge, and because patients may exhibit a late asthmatic response and need to be kept in hospital for at least 24 hours post challenge. The allergen/occupational challenge must be performed in a suitable challenge room, with air extraction, to ensure the subject and staff are not put at risk. Therefore, it is recommended that these tests be only carried out in specialised centers, which have expertise in this particular area. Because these types of challenge test are not widely available in the UK they will not be covered further.

The types of challenge testing undertaken routinely can be split broadly into two groups, a) those eliciting a response using a pharmacological agent and b) those that use physical stimuli. These groups can be further classified into a) agents that work either directly or indirectly to cause bronchospasm and b) exercise challenge, inhalation of cold dry air and aerosolised mannitol (a carbohydrate which reacts osmotically on the airways).

Commonly used pharmacological agents that work directly on the bronchial smooth muscle are methacholine and histamine. Agents that work indirectly and cause bronchoconstriction by

triggering mediator release from cells include adenosine 5 – monophosphate, bradykinin, tachykinins, leukotrienes and sodium metabisulphite are mainly used in research.

The results from the various challenge tests are only weakly correlated and therefore, are not interchangeable. Each challenge gives different but often complementary information on the different pathways that cause airways narrowing.

Table 7.1 Definition of terms used in challenge testing

Abbreviation	Definition	Units (if applicable)
BHR	Bronchial hyperresponsiveness	Not applicable
AHR	Airways hyperresponsiveness	Not applicable
Raw	Airways resistance	$KPa.l_{-1}.s$
SGaw	Airways conductance	$s^{-1}.kPa_{-1}$
PC_{20}	Provocative concentration (the concentration that gives a 20% or> drop in FEV_1)	mg/ml
PD_{20}	Provocative dose (the concentration given x the number of breaths cumulatively added at each level that gives a 20% or > drop on FEV_1)	mg/ml
EIA	Exercise induced asthma	Not applicable
EIB	Exercise induced bronchoconstriction	Not applicable
Provocholine	Metapharm trade name for methacholine chloride	Not applicable
MMD	Mass median diameter (relates to particle size)	microns
AMP	Adenosine monophosphate	N/A
PEFV	Partial expiratory flow/volume curve	N/A
$tPaO_2$	Transcutaneous Oxygen	kPa
MVV	Maximum voluntary ventilation	L/min
VAS	Visual analog scale	N/A
Hyper-reactivity	Subject has an increased reaction to the stimuli and there will be a large drop in FEV1 when the airways react, i.e. the more reactive the greater the bronchoconstriction	N/A
Hyper-sensitivity	Subject has greater sensitivity to the stimuli i.e. will react at lower doses (concentrations) of the stimuli	N/A