

Figure 2 Tumour invading the pleura (\*, arrows) and encroaching the blood vessel (BV, arrowheads). The tumour cells (insert) are columnar or cuboidal in shape and arranged in a typical bronchioloalveolar pattern. Stain: haematoxylin and eosin.

tured” into the pleural cavity causing the haemothorax. The latter possibility appears likely as examination of the resected specimen showed a small perforation in the vis-

ceral pleura which was covered by a fibrin clot, and microscopic examination revealed tumour invasion of the pulmonary vessels and visceral pleura (fig 2).  
To our knowledge this is the first report of primary lung cancer causing haemothorax.

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# Need for a comparative performance standard for dry powder inhalers

Robert Richards, Michael Saunders

## Abstract

The efficacy of dry powder inhalers is dependent on the inspiratory flow rate at which they are used. The resistance to airflow through five different dry powder inhaler devices was measured. The devices were shown to vary significantly, with the Turbohaler having the highest resistance. We suggest that the performance of dry powder inhalers should be assessed at comparable pressure drops producing clinically relevant inspiratory flow rates for each device.

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Department of Respiratory Medicine, Llandough Hospital, Cardiff CF6 1XX  
R Richards  
M Saunders  
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There are now five types of dry powder inhaler (DPI) available for prescription in the United Kingdom. At present there is no measure of performance by which comparisons of DPIs can be made and no official guidelines have been published.  
Most DPIs are sensitive to inspiratory flow rate, the higher the flow rate the greater the efficacy of drug delivery.<sup>1-4</sup> All standard pulmonary function tests are poor predictors of the inspiratory flow rate that patients can

generate through these devices.<sup>5</sup> To demonstrate the wide differences between the devices we have measured the resistance of the Turbohaler, Diskhaler (four and eight place), Rotahaler, and Spinhaler.

## Methods

The resistance of each DPI was assessed using a static tube and water manometer employing the method described by Cotes<sup>6</sup> (fig 1). Each DPI was loaded and actuated as described in the written instructions and then attached to one end of the static tube. The air flow was generated by an electrically driven blower, adjusted via a choke valve, and measured by a rotameter. One end of a water manometer was inserted into the static tube with the other end being open to the atmosphere, enabling the pressure drop caused by each device to be measured at specific flow rates. Each device was assessed from 10 l/min with increasing increments of 10 to a maximum of 100 l/min. Three measurements were made at each flow rate for each device. Differences between the data points were assessed by analysis of variance.

## Results

Each device has its own pressure/flow characteristics (fig 2). Variation in the measurements were minimal with all standard deviations being under 12 mm H<sub>2</sub>O. The device with the least resistance was the Spinhaler which, at 60 l/min, had a mean (SD) deflection of only 35 (0.58) mm H<sub>2</sub>O. All the other devices had significantly greater

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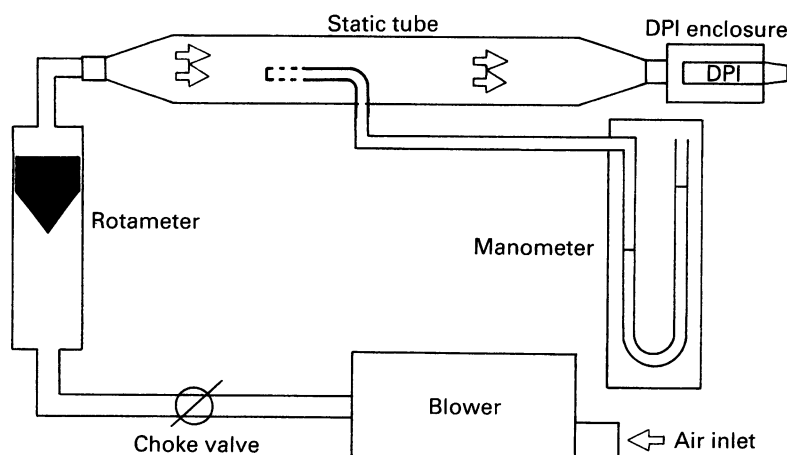


Figure 1 The device used to compare the pressure drop across the dry powder inhalers. Adapted from Cotes.<sup>6</sup>

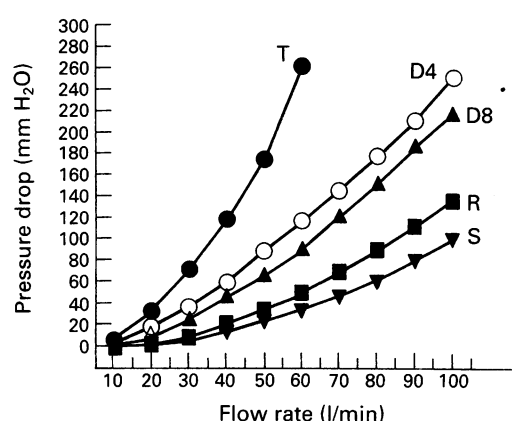


Figure 2 Mean pressure/flow relationship of five dry powder inhalers. T—Turbohaler (●); D4—Diskhaler four place (○); D8—Diskhaler eight place (▲); R—Rotahaler (■); S—Spinhaler (▼).

resistances at flow rates above 20 l/min ( $p < 0.01$ ) than the Spinhaler, with the Turbohaler having the highest (fig 2). In practice a patient would have to be capable of much higher pressures to achieve these flow rates, so they cannot be directly translated into values for maximum inspiratory pressures and are therefore suitable for comparative purposes only.

### Discussion

We have shown a wide variation in the resistances of DPIs. It is probable that the dispersion of the powder into an aerosol is dependent on the turbulence created by the DPI and not the absolute flow rate, but for each device the turbulence would be proportional to the inspiratory flow rate. When

choosing a DPI for a patient one is faced with a wide choice. It is possible to deliver both  $\beta_2$  agonists and corticosteroids via three types of DPI (Rotahaler and Diskhaler (eight place): Allen and Hanburys Ltd; Turbohaler: Astra Pharmaceuticals Ltd). If the performance of these devices was assessed at 60 l/min, as is the case for metered dose inhalers,<sup>7</sup> the wrong impression would be given as to their function in the clinical setting. To achieve 60 l/min through a Turbohaler would take nearly three times the effort needed for the eight place Diskhaler (264 mm H<sub>2</sub>O v 90 mm H<sub>2</sub>O). Comparable data on these devices would be best obtained at a series of constant pressure drops—for example, at 100 and 200 mm H<sub>2</sub>O—thereby providing a guide to the relative performance in clinical practice. For example, a patient who could achieve an inspiratory flow rate of 35 l/min through a Turbohaler could manage over 80 l/min via a Rotahaler; at present we do not know which device would be the more effective at these flow rates. Adoption of this form of testing would take into account the greater inertial impaction produced at high flow rates as the specific flow rate used would be similar to that produced in the clinical setting. However, impaction is probably of less importance than the raw inspiratory flow rate, as we have shown previously that flow rates of up to 300 l/min produce both superior drug delivery and protection when using the Spinhaler.<sup>12</sup>

In the case of  $\beta_2$  agonists it is usually obvious if a particular device is ineffective in an individual patient. However, we are more concerned with the use of corticosteroid DPIs where no immediate feedback is given as to the efficacy of the inhalation. It is therefore important that data be provided by the manufacturers of these devices so that useful comparisons can be made and the right device can be prescribed for the individual patient.

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