

# Measurement of nasal potential difference in adult cystic fibrosis, Young's syndrome, and bronchiectasis

E W F W ALTON, J G HAY, C MUNRO, D M GEDDES

From Brompton Hospital, London

**ABSTRACT** Previous work confirmed the abnormal potential difference between the undersurface of the inferior nasal turbinate and a reference electrode in cystic fibrosis, but the technique is difficult and the results show overlap between the cystic fibrosis and the control populations. In the present study the potential difference from the floor of the nose has therefore been assessed in normal subjects, as well as in adult patients with cystic fibrosis, bronchiectasis and Young's syndrome. Voltages existing along the floor of the nasal cavity were recorded. The mean potential difference was similar in controls ( $-18$  (SD 5) mv) and in patients with bronchiectasis ( $-17$  (6) mv) and Young's syndrome ( $-20$  (6) mv). The potential difference in cystic fibrosis ( $-45$  (8) mv) was significantly different from controls ( $p < 0.002$ ) and there was no overlap between the cystic fibrosis values and values obtained in normal and diseased controls. This simple technique therefore discriminates well between patients with cystic fibrosis and other populations, raising the possibility of its use to assist in diagnosis.

It has been known since the turn of the century that certain epithelial cells are capable of generating and maintaining potential differences across their surfaces. Attention was not focused on the respiratory tract, however, until the 1970s; initially *in vitro*<sup>1</sup> and later *in vivo*<sup>2,3</sup> studies on the dog trachea showed that similar voltages could be recorded. Melon<sup>4</sup> in 1968 had shown that the excised lining of the human nose has a spontaneous potential difference, and since the histological appearances of the upper and lower respiratory tract are very similar it became a logical next step to measure human nasal potentials *in vivo*, this being first achieved by Knowles and colleagues in 1981.<sup>5</sup>

Since active ion transport may be important in determining both the volume and the composition of the airways' surface liquids, and since it is suspected that both of these may be abnormal in cystic fibrosis, nasal potentials have been studied in this population. Knowles measured the voltages existing along the undersurface of the inferior turbinate (fig 1), and showed that patients with cystic fibrosis show substantially more negative potentials than healthy controls.<sup>6</sup>

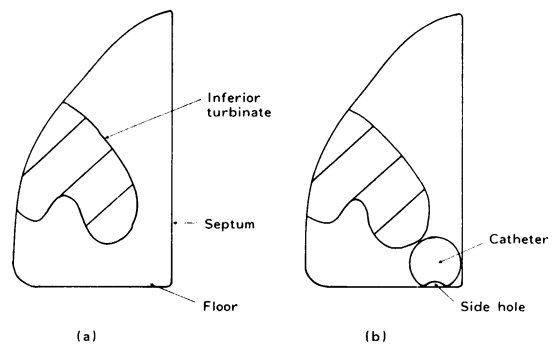


Fig 1 Right nasal cavity (a), with catheter *in situ* (b).

We have been able to repeat these studies<sup>7</sup> but find the technique both difficult and time consuming, with overlap of values between controls and patients with cystic fibrosis. Furthermore, few of our volunteers were keen to return for repeat readings. Clearly, if such a technique is to become widely used it must be easily learnt with relatively little specialised training, and be well tolerated by the subject.

In the present study both equipment and site of measurement have been altered to produce a technique that is rapid, easily performed, and well tolerated. To determine whether the abnormal potential in cystic fibrosis is related to problems with mucus clearance or chronic infection, two further populations

Address for reprint requests: Dr E W F W Alton, Brompton Hospital, London SW3 6HP.

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were studied—patients with Young's syndrome and a group with bronchiectasis secondary to childhood illness or of unknown aetiology.

## Methods

### SUBJECTS

We studied the following four groups of subjects:

*Twenty patients with cystic fibrosis*, 10 male and 10 female, with a mean age of 25 (range 17–37) years. Each had been diagnosed according to clinical and radiological criteria and all had been found to have an abnormal sweat sodium value. The severity of disease varied from requirement for regular hospital admission to outpatient follow up only.

*Twelve patients with bronchiectasis*. In six this was related to childhood measles or whooping cough and in six it was of unknown aetiology. All showed consistent changes on chest radiographs and bronchograms and all reported chronic production of purulent sputum.

*Seven male patients with Young's syndrome*. All seven suffered from repeated upper and lower respiratory tract infections, were infertile, and showed prolonged mucociliary clearance of a nasal saccharine tablet.

*Twenty healthy controls*, 10 male and 10 female, with a mean age of 29 years (range 23–35). All were non-smokers, none was taking any medication other than an oral contraceptive, and none gave a history of atopy or acute or chronic rhinitis.

### EQUIPMENT

The reference electrode consisted of a 20 gauge Venflon (Viggo) cannula placed subcutaneously in the

forearm and perfused slowly with Ringer's saline (Travenol). This was connected to a high impedance voltmeter ( $10^{11}$  ohms) by means of a saturated potassium chloride bridge and calomel cell. The recording electrode was a size 8 Foley catheter similarly perfused with Ringer's saline and used without inflation of the end balloon. Contact with the floor of the nasal cavity was made through a side hole at the tip of the catheter (fig 1) and connection to the voltmeter was established as for the reference electrode. A permanent record was produced by a Devices recorder attached to the voltmeter.

Recordings were taken from the floor of the nasal cavity at approximately 1 cm intervals, the site being visualised with the aid of an auroscope speculum and otolaryngologist's light. The maximum stable potential ( $\pm 0.5$  mv over 10 seconds) was noted on two occasions from each side of the nose and the mean maximum value was used in the analysis. The electrodes were tested for asymmetry before and after examination of each subject, an acceptable value being a difference of 0.5 mv. The Mann-Whitney U test was used in the statistical analysis of the data.

## Results

The mean (SD) potential difference from 20 patients with cystic fibrosis was  $-45$  (8) mv and that of the controls was  $-18$  (5) mv (fig 2). There was no overlap between the results from the two groups and the Mann-Whitney U test showed the difference to be highly significant ( $p < 0.002$ ). Patients with Young's syndrome had a mean potential difference of  $-20$  (6) mv and patients with bronchiectasis  $-17$  (6) mv, values that were not significantly different from those obtained in the controls. Again no overlap was noted between results from either group and those from subjects with cystic fibrosis.

To ensure that the abnormal potentials were not caused by drugs taken by the patients we reanalysed these data taking into account the drugs used. Within each type of treatment there was no trend towards either lower or higher potentials.

There was no correlation between potential difference and sweat sodium concentration measured at any time in the patient's lifetime. Neither was there a relationship between potential difference and severity of the disease measured subjectively.

Of the 59 subjects studied, one suffered a vasovagal episode on insertion of the subcutaneous cannula; but there were no other unwanted effects.

## Discussion

We have previously confirmed the increased negative potential along the undersurface of the inferior tur-

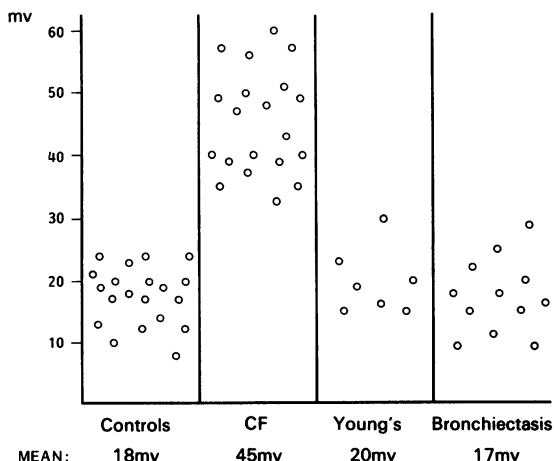


Fig 2 Potential recordings (in millivolts (mv), lumen negative) in control subjects and in patients with cystic fibrosis, Young's syndrome, and bronchiectasis.

binate in patients with cystic fibrosis.<sup>7</sup> We found, however, that the results overlapped those obtained in normal controls, in part at least because of technical difficulties. Because no site other than the nose could be shown to have the desired specificity, and as the method was time consuming and in some cases uncomfortable for subjects, it was concluded that the technique might have little diagnostic value.

A more readily accessible part of the nose is that area bounded by the septum medially and the inferomedial border of the inferior turbinate laterally, here referred to as the floor of the cavity (fig 1). The mean (SEM) values of potential difference for this region,  $-20.6(3.2)$  mv for woman and  $-14.7(3.2)$  mv for men, recorded in controls in Knowles's study,<sup>5</sup> are very much in keeping with our own. The shape of the potential difference profile from this region is also similar to that recorded from the undersurface of the inferior turbinate,<sup>5</sup> the maximum value obtained being at about 1.5–2 cm behind the anterior tip.

The use of a soft, flexible exploring electrode, without the need for agar, has allowed increased stability of potential difference recordings (with typical values of  $\pm 0.3$  mv over 15 seconds), greater comfort for the subject, and more rapid measurement. This region of the nose has never, to our knowledge, been shown to have the increased potential difference characteristic of cystic fibrosis, yet it is easily accessible and the results show no overlap of values between controls and patients with cystic fibrosis. Apart from one needle related syncopal episode no unpleasant effects were noted, and we therefore conclude this is a rapid and well tolerated technique. So far it shows high degrees of both sensitivity and specificity and is easily performed without the need for specialised training.

Five patients with cystic fibrosis, each having recently undergone a sweat test, were asked to compare the two methods. Although we clearly appreciate the bias introduced by our questioning, it is nevertheless worthy of note that each expressed a preference for nasal potential difference recordings as the less unpleasant of the techniques. It is perhaps not surprising that sweat sodium measurements, some obtained many years previously, bore no relationship to nasal potential differences.

Patients with cystic fibrosis are prone to recurrent infections, and are also thought to have reduced mucus clearance; so the abnormal potential difference could be related to either factor. Skin potentials are crucially dependent on sweat duct activity and corneal hydration, and denuded areas of ciliated respiratory epithelium show substantially altered potential differences. Patients with Young's syndrome have abnormal mucus clearance despite normal ciliary activity, are infertile, and suffer from repeated upper and lower respiratory tract infections. They therefore resemble patients with cystic fibrosis in many ways,

but they have normal sweat sodium measurements. Our seven patients had potential differences that were no different from those of controls.

The 12 subjects with bronchiectasis suffered from continuous production of purulent sputum with frequent exacerbations requiring inpatient treatment. All had normal mucociliary function as judged by clearance time of a saccharine tablet placed in the nasal cavity. Again, none showed any significant change in potential difference.

Quinton, from his elegant studies on sweat ducts both *in vivo*<sup>8</sup> and *in vitro*,<sup>9</sup> has suggested that chloride impermeability may be responsible for the increase in potential difference, while Knowles and colleagues<sup>6</sup> consider that abnormal sodium fluxes may also contribute to these values. The increased potential difference does not appear to be secondary to chronic infection or mucus transport problems, and it is easy and quick to record. The possibility of using nasal potential difference as an adjunct to established means of diagnosis for cystic fibrosis requires the testing of larger numbers, especially among infants and children.

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