

than as a circulating hormone involved in cardiovascular homeostasis. Thus, measurement of plasma CNP levels and studies involving systemic infusions of CNP may have only a limited role in clarifying its physiological significance.

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- Komatsu Y, Nakao K, Suga S, Ogawa Y, Mukoyama M, Arai H, *et al.* C-type natriuretic peptide in rats and humans. *Endocrinology* 1991;129:1104-6.
- Stingo AJ, Clavell AL, Heublein DM, Wei C, Pittelkow MR, Burnett JC. Presence of C-type natriuretic peptide in cultured human endothelial cells and plasma. *Am J Physiol* 1992;263:H1318-21.
- Suga S, Nakao K, Itoh H, Komatsu Y, Hama N, Imura H. Endothelial production of C-type natriuretic peptide and its marked augmentation by transforming growth factor  $\beta$ . *J Clin Invest* 1993;90:1145-9.
- Koller KJ, Lowe DG, Bennett GL, Minamino N, Kangawa K, Matsuo H, *et al.* Selective activation of the B-natriuretic peptide receptor by C-type natriuretic peptide (CNP). *Science* 1991;252:120-3.
- Stingo AJ, Clavell AL, Aarhus LL, Burnett JC. Cardiovascular and renal actions of C-type natriuretic peptide. *Am J Physiol* 1992;262:H308-12.
- Wei CM, Heublein DM, Perrella MA, Lerman A, Rodeheffer RJ, McGregor CGA, *et al.* Natriuretic peptide system in human heart failure. *Circulation* 1993;88:1004-9.
- Lang CC, Coutie WS, Struthers AD, Dhillon DP, Winter JH, Lipworth BJ. Elevated levels of brain natriuretic peptide in acute hypoxaemic chronic obstructive pulmonary disease. *Clin Sci* 1992;83:529-33.
- Burnett JC, Kao PC, Hu DC, Heger D, Heublein D, Granger J, *et al.* Atrial natriuretic peptide elevation in congestive heart failure in the human. *Science* 1986;231:1145-7.
- Cargill RI, Coutie WJ, Lipworth BJ. The effects of angiotensin II on circulating levels of natriuretic peptides. *Br J Clin Pharmacol* 1994;38:139-42.
- Baertschi A, Adams JM, Sullivan MP. Acute hypoxaemia stimulates atrial natriuretic factor secretion *in vivo*. *Am J Physiol* 1988;255:H295-300.

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## Effect of exercise on the nasal transmucosal potential difference in patients with cystic fibrosis and normal subjects

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Mean (SE) effects of exercise on the nasal transmucosal potential difference in patients with cystic fibrosis and controls

	Before exercise	After exercise	Greatest change after exercise	Recovery
Cystic fibrosis (n=7)	-27.6 (5.8)	-17.7 (5.2)†	-16.6 (5.5)†	-32.6 (5.9)
Controls (n=7)	-12.0 (2.1)	-19.8 (2.4)†	-22.1 (3.2)†	-17.2 (2.8)

\* Differences within columns ( $p < 0.05$ )

† Differences between resting and subsequent values within rows ( $p < 0.05$ ).

### Abstract

**Background** - Normal subjects have a negative nasal transmucosal potential difference (TPD) at rest which becomes more negative with exercise. Patients with cystic fibrosis have a more negative resting nasal TPD than controls. The present study was designed to determine the effects of exercise on the TPD of patients with cystic fibrosis.

**Methods** - Seven subjects with cystic fibrosis and seven control subjects had their usual TPD measured at rest, and during and after a 12 minute period on an exercise bicycle designed to produce a pulse rate of 80% of their maximum predicted value. **Results** - The normal subjects developed a more negative nasal TPD during exercise which returned towards normal at the completion of the rest period. The patients with cystic fibrosis had higher resting values which became less negative during exercise. At the end of the exercise period there was no difference between the two groups. At the end of the recovery period

the results for the patients with cystic fibrosis had returned to their resting values. **Conclusions** - Exercise reduces the abnormally high resting values for nasal TPD in patients with cystic fibrosis. Elucidation of the mechanism for this change may help to produce functional improvement for patients with this disease.

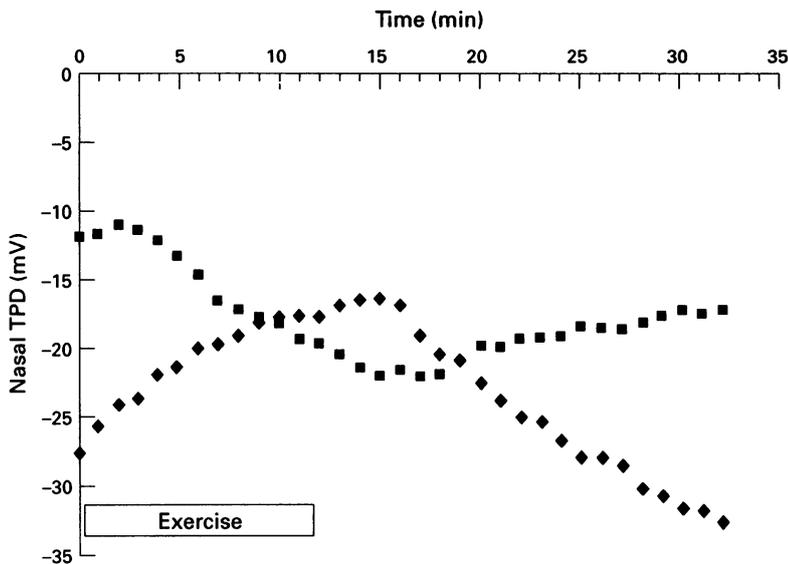
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Cystic fibrosis is characterised by an increase in thick mucous secretions. A defective transmembrane regulator for chloride transport in epithelial cells, unable to open under the influence of cyclic AMP, has been described.<sup>1</sup> Respiratory epithelial cells from patients with cystic fibrosis also have a high sodium absorption from the mucosal surface which causes a more negative transmucosal potential difference (TPD) than in controls.<sup>2</sup>

Exercise causes an increase in nasal secretion in normal subjects.<sup>3</sup> TPD also increases in normal subjects during exercise, a change probably related to the increase in secretion.<sup>4</sup> The current study was performed to see if the nasal TPD behaved in the same way during exercise in patients with cystic fibrosis and healthy subjects.

### Methods

Seven patients with cystic fibrosis (four men) aged 9-24 years and seven age and gender matched healthy controls volunteered for the



Effect of 12 minutes of exercise on the mean nasal transmucosal potential difference (TPD) in seven patients with cystic fibrosis (◆) and seven healthy controls (■).

study which was passed by the ethical committee of the Queen's University, Belfast. The mean Schwachman-Kulczycki clinical score of the patients was 64 (range 34–92).

Exercise was performed for 12 minutes on a bicycle and set at a work level to achieve 80% of their predicted maximum heart rate.

The nasal TPD was measured using a soft rubber catheter as the exploring electrode, the reference electrode being placed over an area of abraded skin.<sup>5</sup> The nasal electrode was placed on the floor of the nasal cavity and kept in place at the site of maximum negative potential difference by tape at the anterior nares. The catheter well was kept filled with electrolyte gel throughout the study. The mean potential difference values over the last 10 seconds of each minute were computed using an Amstrad computer with an SIEM-3 program. All subjects rested for 30 minutes before the study and the catheter was inserted 10 minutes before exercise began. Twelve minutes of exercise were followed by 20 minutes of rest.

Statistical analysis was by paired *t* testing, a probability level of  $p < 0.05$  being accepted as a statistically significant result.

## Results

The results are as shown in the table. There was a significant difference between the resting nasal TPD for the two groups of subjects, the patients with cystic fibrosis being more negative. During exercise (figure) the values for the patients with cystic fibrosis became relatively more positive and at the end of exercise these were significantly different from the resting values ( $p < 0.05$ ). At the end of the rest period the values increased to become more negative and they were not significantly different from the pre-exercise values. In the control subjects, however, the nasal TPD increased to become more negative with exercise. This increase was significant ( $p < 0.05$ ) and, at that stage, was not significantly different from that for the patients with cystic fibrosis. After exercise the control values diminished towards the resting ones.

## Discussion

The resting values for nasal TPD for the patients with cystic fibrosis and the controls were significantly different in this study and were within the range of other published values.<sup>3,5</sup> The alteration in the potential difference with exercise was in the opposite direction in the two groups. Within the two groups and in previous studies there was no evidence of reversion towards the mean in subjects whose resting values were either high or low for the group. We therefore feel that this difference between the groups is a real observation. Although the mechanism of the change in potential difference may be different in the two groups, the actual potential difference was significantly different at the end of exercise.

In exercise increased nasal secretion is needed to humidify the air. Much of this increase in secretion is by parasympathetic nerve stimulation since it can be blocked by ipratropium.<sup>6</sup> Since methacholine also increases the nasal TPD,<sup>4</sup> it is probable that an increased secretion of chloride contributes to the greater negative potential in healthy subjects. In patients with cystic fibrosis, however, the nasal TPD becomes less negative. If chloride channels cannot open properly in the respiratory mucosa, then one would not expect TPD to increase with exercise in cystic fibrosis. Patients with this disease do have a problem with increasing the humidification of dry air,<sup>7</sup> but the clinical observation that they can produce clinical secretions remains. It is therefore possible that the more positive TPD during exercise results from a decrease in their exaggerated sodium ion absorption, especially since the sodium channel blocker, amiloride, can cause this change at rest.<sup>8</sup> The deficient chloride channels can be made to open at rest when cells are stimulated by ATP or UTP following amiloride blockade.<sup>8</sup> Whether or not purinergic receptors are active during exercise in patients with cystic fibrosis or control subjects is not known.

Elucidation of the mechanism of mucosal TPD reduction during exercise in patients with cystic fibrosis may provide a therapeutic option for the treatment of this disease.

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- Li M, McCann JD, Liedtke CM, Nairn AC, Greengard P, Welsh MJ. Cyclic AMP-dependent protein kinase affects chloride channels in normal but not cystic fibrosis airway epithelium. *Nature* 1988;331:358–60.
- Knowles MR, Gatzky JT, Boucher RC. Increased bioelectric potential differences across respiratory epithelia in cystic fibrosis. *N Engl J Med* 1981;305:1489–95.
- Stanford CF, Stanford RC. Exercise induced rhinorrhea (athlete's nose). *BMJ* 1988;297:660.
- Stewart EJ, Cinnamon DM, Nicholls DP, Stanford CF. The effect of methacholine on nasal potential difference. *Rhinology* 1993;31:77–9.
- Alton EFWF, Hay JG, Munro C, Geddes DM. Measurement of nasal potential difference in adult cystic fibrosis, Young's syndrome and bronchiectasis. *Thorax* 1987;42:815–7.
- Harris W, Giebaly K, Adair C, Adair C, Al Suwaidan S, Nicholls DP, Stanford CF. The parasympathetic system in exercise induced rhinorrhea. *Rhinology* 1992;30:21–3.
- Primiani FP, Saidel GM, Montagu FW, Kruse KL, Green CG, Horowitz JG. Water vapour and temperature dynamics in the upper airways of normal and CF subjects. *Eur Respir J* 1988;1:407–14.
- Knowles MR, Clarke LL, Boucher RC. Activation by extracellular nucleotides of chloride secretion in the airway epithelia of patients with cystic fibrosis. *N Engl J Med* 1991;325:533–8.