# Familial primary spontaneous pneumothorax consistent with true autosomal dominant inheritance

P J Morrison, R C Lowry, N C Nevin

**Abstract**

**A family exhibiting spontaneous pneumothorax in a father and three offspring (two sons and one daughter) is described. The mode of inheritance is apparently autosomal dominant with two episodes of male to male transmission in one family. The age of onset varied by up to 13 years within the family. Isolated autosomal dominant pneumothorax appears to be a distinct clinical entity.**

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Keywords: pneumothorax, familial, autosomal dominant.

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Most cases of spontaneous pneumothorax are isolated. Familial cases which were first reported by Farber in 1921[1] are rare. In a recent review of the literature 29 families of spontaneous pneumothorax were identified.[2] The mode of inheritance is still unclear. The possibilities include either autosomal dominant with reduced penetrance in females or X-linked inheritance.[2] Familial pneumothorax may be a feature of other Mendelian genetic diseases including $\alpha_1$-antitrypsin deficiency,[3] Marfan syndrome,[4] Ehlers-Danlos syndrome, and other connective tissue disorders.[5]

We describe a family with three affected males (father and two sons) and an affected daughter. In this family autosomal dominant inheritance is confirmed by male to male transmission.

*Table 1 Respiratory function test results*

| *Test* | *Patient III.1* | *Patient III.5* | *Patient III.6* |
|---|---|---|---|
| $FEV_{1.0}$ (l) | 4.25 (115%) | 4.1 (105%) | 3.18 (97%) |
| FVC (l) | 5.0 (112%) | 5.2 (113%) | 3.86 (95%) |
| FEV/FVC% | 85 | 79 | 82 |
| VC (l) | 5.1 (115%) | 5.6 (121%) | 3.8 (94%) |
| FRC (l) | 4.1 | 2.3 | 2.7 |
| RV (l) | 1.6 (91%) | 1.1 (68%) | 1.3 (89%) |
| TLC (l) | 6.8 (107%) | 6.7 (107%) | 5.1 (93%) |
| RV/TLC% | 24 (82%) | 16 (62%) | 26 (102%) |
| TLCO (1) (mmol/min/kPa) | 9.6 (93%) | 11.5 (107%) | 8.1 (86%) |
| TLCO (2) (mmol/min/kPa) | 9.8 (96%) | 11.3 (106%) | 8.0 (85%) |
| KCO (mmol/min/kPa) | 1.6 (95%) | 2.0 (108%) | 1.7 (91%) |

Figures in parentheses are % predicted.
FEV = forced expiratory volume; FVC = functional vital capacity; VC = vital capacity; RV = residual volume; TLC = total lung capacity; TLCO (1) = single breath CO transfer factor using alveolar volume by single breath helium dilution; TLCO (2) = single breath CO transfer factor using alveolar volume from RV obtained by multiple breath helium dilution; KCO = transfer factor per litre of alveolar volume.

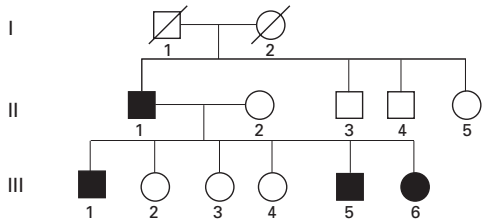


*Figure 1 Three generation pedigree showing affected members (black) and relatives. Patient I.1 had chest pains in his 30s but no further details are known.*

## Case history

Four affected individuals are described. The index case III.1 (fig 1), a male, presented at the age of 30 years with left sided chest pain and shortness of breath. He had no previous history of chest problems although he smoked 20 cigarettes per day. Radiography of the chest confirmed pneumothorax. He was treated with a chest drain and complete resolution occurred with no further episodes. His brother III.5 who was a non-smoker with no previous respiratory problems presented at the age of 21 to his general practitioner with acute shortness of breath. This resolved within 24 hours without intervention. Two months later he had a further episode of shortness of breath and a left sided pneumothorax was diagnosed and confirmed by radiography. A chest drain was inserted and he made a full recovery. Eleven months later he had a recurrence of the pneumothorax which again required a chest drain. Their sister (III.6) presented at the age of 17 with acute shortness of breath and radiography of the chest confirmed left sided pneumothorax. There was re-expansion of the lung without drainage. She had no previous respiratory history and smoked 25 cigarettes per day. Their father II.1 had an acute pneumothorax at the age of 32 years which did not require a drain.

On clinical examination of III.1, III.5, and III.6 there was no evidence of Marfan syndrome, Ehlers-Danlos syndrome, or other connective tissue disorders according to defined diagnostic criteria.[6 7] Examination of the remaining unaffected siblings revealed no difference in body habitus and there were no other differentiating features indicative of respiratory or connective tissue disease. Laboratory investigations including $\alpha_1$-antitrypsin assays were normal. The chest radiographs did not show sharpness of the first or second ribs[8] or of bullae or other lung malformations. Respiratory function tests including diffusion studies were all within normal limits (table 1).

## Discussion

Familial pneumothorax is rare and may often be a pointer to an unrecognised connective tissue disorder. Abolnick *et al*[2] described 15 families with familial pneumothorax in a retrospective survey of men in the Israeli Defence Force. He also reviewed all the additional families previously published in the medical literature with sufficient information to construct a pedigree. A total of 14 families was found,

giving an overall total of 29 families for analysis. Two possible modes of inheritance were suggested from this study – autosomal dominant (AD) with reduced penetrance in females and X-linked recessive (XLR) inheritance. Autosomal recessive inheritance was thought to be very unlikely.

The authors found differences between the AD and XLR forms with possible earlier onset in the XLR form and more frequent episodes in the AD form. The family described here clearly has autosomal dominant pneumothorax with no clinical features to suggest a co-existing connective tissue disorder. We were unable to find any specific physical differences between affected and unaffected family members. Even within this family the clinical expression is very variable with onset in the sister (III.6) at 17 years, in the index case (III.1) at 30 years, and recurrence in the other brother (III.5). The associated effects of smoking and other environmental factors cannot be accurately assessed.

The variability within this family is consistent with an autosomal dominant gene with variable penetrance. We conclude that autosomal dominant pneumothorax is a definite entity and most of the cases reviewed by Abolnick *et al*[2] are inherited in an autosomal dominant mode with variable penetrance. In some families X-linked inheritance cannot be excluded. Further careful documentation of families with spontaneous pneumothorax may provide clarification in the future.

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# Can reactive airways dysfunction syndrome (RADS) transform into occupational asthma due to "sensitisation" to isocyanates?

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**Abstract**

**The case history is described of a worker who presented with a history suggestive of reactive airways dysfunction syndrome which occurred after an acute high level inhalation of diphenylmethane diisocyanate. Further exposure at work, at a time when concentrations of isocyanates were no longer "irritant", suggested occupational asthma; this diagnosis was confirmed by a specific inhalation challenge test.**

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Keywords: occupational asthma, reactive airways dysfunction syndrome, isocyanates.

Isocyanate exposure in the work place is the most frequent cause of occupational asthma.[1] By contrast, only few cases of reactive airways dysfunction syndrome (RADS), a distinct type of occupational asthma without a latency period,[2] have been related to a brief high level exposure to isocyanates.[3–7] We report a case of occupational asthma to diphenylmethane diisocyanate (MDI), documented by a specific bronchoprovocation challenge test, which might have been initiated by a history suggesting RADS. This observation suggests that "sensitisation" may develop as a result of an intense exposure, and demonstrates the need for objective testing before re-exposure to the offending agent in the case of concomitant chronic exposure at low levels.

## Case report

A 54 year old man was hired to work in a foundry in 1993. He had a 30 pack year history of smoking and no personal history of asthma or atopy. His job consisted of making cores which involved frequent exposures to MDI. In March 1996 an accidental spill of a large volume of solvent containing MDI occurred in his work area. He was off duty during the spill and returned to work 48 hours later. There was a strong and irritant smell in the plant and within one hour he experienced headache, sore throat, cough, and chest tightness. Other workers in this area reported the same symptoms that were, however, transient. His chest symptoms increased gradually and a month later he consulted his physician. He then noticed that wheeze and chest tightness worsened at work and improved during weekends. He was put on sick leave and salbutamol was administered on an as needed basis without significant relief. In May 1996 a spirometric test revealed moderate airflow obstruction with a forced expiratory volume in one second ($FEV_1$) of 2.5 l