Field trial of a rapid card test for *Wuchereria bancrofti*

David O Freedman, Adriana de Almeida, Janaina Miranda, D Adam Plier, Cynthia Braga

Elimination of lymphatic filariasis, which infects 120 million people worldwide, is now thought to be feasible.[1] In order for control programmes to be designed around a strategy of community diagnosis and repeated annual mass chemotherapy, efficient surveillance procedures will be needed.[2] Testing for circulating filarial antigen has now emerged as the method of choice for the detection of *Wuchereria bancrofti* infections.[3] ELISA-based antigen testing can be done on blood collected at any time of day or night, but is not easy to do in the field. In retrospective testing of frozen serum, a self-contained 5 min immunochromatographic card test for filarial antigen (ICT Diagnostics, Balgowlah, Australia) has been shown to be comparable to ELISA.[3] We report on a trial of the card test under field conditions.

We studied 847 residents of a *W bancrofti*-endemic community of Recife, Brazil. In the card test, 50 μL of untreated daytime serum are added to a small pad on the 7·5×6·5 cm card which has dried colloidal-gold-labelled polyclonal antifilarial antibodies. Addition of two drops of buffer to the card allows antibody and antigen (if present) to flow across a nitrocellulose strip precoated with a monoclonal antifilarial antibody. Positive serum samples cause a pink line that is read by eye in the field and each card is labelled as a permanent record. Specificity of the card test has been shown to be greater than 99%.[3] Prevalence of infection in men and women was higher than had previously been reported from any community in the greater Recife area (table).[4] Further blood was obtained from a sample of those studied with both positive and negative card tests for direct comparison with other methods. Had we conducted the survey with the surveillance technique most widely used in control programmes—examination of stained thick films of night blood specimens—we would have underestimated infection prevalence by more than four-fold in this population. Use of the more cumbersome technique of membrane filtration of night blood specimens decreased sensitivity by 50%. The card test was slightly less sensitive than ELISA. Serum that had been tested then frozen and thawed gave the same results when re-tested by card assay.

The rapid card test for filarial antigen requires no additional equipment, so can be carried out under true field conditions. The test should facilitate implementation of new strategies proposed by WHO for the control and elimination of lymphatic filariasis.[2]

This work was supported by grant AI-31552 from the US National Institutes of health.

1 CDC. Recommendations of the international task force for disease eradication. *MMWR* 1993; **42** (RR-16): 1–25.

	Men	Women	Total
Infection prevalence (card positivity; %)	69/266 (25·9)	82/581 (14·1)	151/847 (17·8)
Age, all (mean; range in yr)	29·5 (4–80)	33·6 (5–85)	32·3 (4–85)
Age, testing positive	28·3 (6–66)	27·6 (8–70)	27·9 (6–70)
	Positive card test*	**Negative card test†**	
Thick-film positive[5]	7/29	0/4	
Membrane-filtration positive[5]	10/20	Not done	
ELISA positive (TropBio, Australia)	43/43	2/34	
Post-thaw card test positive	31/31	0/13	

*Denominator is sample of individuals who tested positive by card test. †Denominator is sample of individuals who tested negative by card test.

Performance of filariasis antigen card test

2 Strategies for control of lymphatic filariasis infections and disease: report of a WHO/CTD/TDR consultative meeting held at the Universiti Sains, Penang, Malaysia, Aug 22–24, 1994. Geneva: WHO, 1994: (TDR/CTD/FIL/Penang/94.1).

3 Weil GJ, Lammie PJ, Weiss N. The ICT filariasis test: a rapid format antigen test for diagnosis of bancroftian filariasis. *Parasitology Today* 1997; **13:** 401–04.

4 Maciel A, Rocha A, Belizia K, et al. Epidemiological study of bancroftian filariasis in Recife, Northeastern Brazil. *Mem Inst Oswaldo Cruz* 1996; **91:** 449–55.

5 Freedman DO, de Almeida PJ, Besh S, et al. Abnormal lymphatic function in presymptomatic bancroftian filariasis. *J Infect Dis* 1995; **171:** 997–1001.

Division of Geographic Medicine, University of Alabama at Birmingham, Birmingham, Alabama 35294, USA (D O Freedman)**; and Centro de Pesquisas Aggeu Magalhaes, Fundacao Oswaldo Cruz, Recife, Pernambuco, Brazil**

Exhaled nitric oxide during lung transplantation

Nándor Marczin, Bernhard Riedel, Janos Gal, Julia Polak, Magdi Yacoub

In lung transplantation, the lungs are vulnerable to injury during harvesting, preservation, and reperfusion.[1] The mechanisms of this injury may involve the lung's capacity to generate nitric oxide (NO).[2] Production of NO contributes to co-ordination of ventilation/perfusion and to host defence by interference with bacterial and viral growth, or to regulation of inflammatory processes.[3] Inhalation of NO in lung-transplant recipients has been reported to be associated with favourable pulmonary haemodynamics, gas exchange, reduced duration of mechanical ventilation and mortality.[4] However, little is known about endogenous NO production. We monitored the exhaled NO concentrations intra-operatively and postoperatively in lung transplantation.

Breath-to-breath analysis of airway NO concentration was with a real-time, computer-controlled, and integrated system (Logan Research Ltd 2000 series). For the duration of the measurement, ventilation was standardised and NO and cabon dioxide were sampled for 80 s as we have previously described.[5] Five representative cycles were analysed for peak (NO_P) or mean exhaled NO levels (NO_M).

We studied 17 patients undergoing lung transplantation who had cystic fibrosis, Eisenmenger's syndrome, primary pulmonary hypertension, sarcoidosis, histiocytosis X, or emphysema. They received either heart-lungs (ten), sequential bilateral lungs (five), or single-lung allografts (two) from cadavers. The donors (mean age 34·3 years) had subarachnoid haemorrhage, primary brain tumour, or traumatic head injury. To investigate the effects of harvesting, preservation, and reperfusion on exhaled NO, measurements were made after completion of the airway anastomoses both before and after reperfusion of the pulmonary vascular bed. Patients undergoing open-heart surgery for coronary bypass grafting served as controls with measurements done before, during, and after cardio-pulmonary bypass.

Baseline intraoperative exhaled NO in the native lungs of the transplant recipients were variable. Patients with cystic fibrosis and one patient with histiocytosis had very low NO. By contrast, patients with Eisenmenger's syndrome or primary pulmonary hypertension had high exhaled NO (NO_P: 6·7 [SD 1·6] ppb; NO_M: 3·9 [0·9] ppb). Analysis of exhaled NO before and after reperfusion of the vascular bed of the donor lungs showed three types of responses. Type I response was characterised by a detectable NO signal before reperfusion (n=4/17; NO_P: 2·0 [0·3] ppb; NO_M: 1·4 [0·2] ppb) which remained unchanged during reperfusion and 24 h after early postoperative period (NO_P: 2·3 [0·4] ppb;

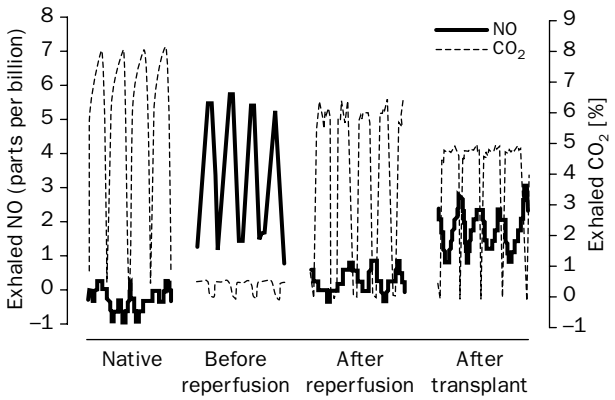

Figure 1: **Representative type II response of exhaled NO and CO2 in a heart-lung transplant recipient for cystic fibrosis**
Traces depict: low exhaled NO levels by the native lungs of the recipient; normal NO levels by the transplanted lungs before reperfusion (exhaled CO2 levels are low because of cardiopulmonary bypass); diminshed NO levels post reperfusion; and partial recovey 24 h after transplantation.

NO_M: 1·5 [0·3] ppb). In type II responses (n=4/17) NO was detected before reperfusion (NO_P: 4·8 [1·2] ppb; NO_M: 3·1 [0·8] ppb), however, reperfusion diminished exhaled NO (NO_P: 1·1 [0·4] ppb; NO_M: 0·7 [0·4] ppb, $p<0·05$, figure). This attenuation was transient, because NO tended to increase towards prereperfusion levels within 24 h (NO_P: 2·5 [0·3] ppb; NO_M: 1·5 [0·1] ppb, figure, post-transplant). Patients with type III responses (n=9/17) had low exhaled NO both before and after reperfusion (NO_P: 0·7 [0·1] ppb; NO_M: 0·3 [0·1] ppb). In these patients, a gradual recovery of exhaled NO levels was seen in the postoperative period (3–14 days). We measured exhaled NO in patients undergoing open-heart surgery before, during, and after cardiopulmonary bypass (CPB). All ten patients investigated had a type I response with no change of exhaled NO during and after CPB bypass (NO_P: 9·0 [1·5] ppb and 8·1 [1·1] *vs* 8·2 [1·6] ppb and NO_M: 5·7 [1·0] and 4·6 [0·6] *vs* 4·7 [1·0] ppb, respectively).

Alveolar-arterial oxygen concentration gradient (measured 6 h after transplantation) was 96 (41–150), 326 (135–537), and 352 (100–642) mm Hg for patients with type I, II, and III responses. No patient died in type I, whereas mortality was one (25%) of four and three (33%) of nine in type II and type III, respectively. Among the surviving patients, the average requirement for mechanical ventilation was 19·5 (8–31), 37 (4–79), and 121 (1–500) h for type I, II, and III. Similarly, average intensive-care unit stay was 45 (34–52), 63 (21–91), and 252 (32–1032) h in these patients. Two patients required NO inhalation for severe allograft dysfunction in type III category, whereas this was not judged to be necessary in any of the patients with type I and II responses.

This study suggests that during the perioperative period, endogenous production of NO by cadaver lung allografts is substantially diminished and follows one of three patterns which appears to correlate with clinical behaviour. Perioperative monitoring of exhaled NO might provide a useful new method for the assessment of donor preservation and evaluating strategies to modulate reperfusion injury. Furthermore, the loss of NO in the perioperative period may provide a rationale for interventions aimed at restoring endogenous NO production or replenishment by intravenous NO donors or inhaled exogenous NO.

N Marczin has been partially supported by the British Heart Foundation during these studies (BHF Project Grant PG/96031). M Yacoub is a British Heart Foundation Professor of Cardiothoracic Surgery. The contribution of the Julia Polak Transplant Fund is greatly appreciated. We thank the consultants, junior doctors, and theatre staff of Harefield Hospital.

1 Pinsky DJ. The vascular biology of heart and lung preservation for transplantation. *Thromb Haemost* 1995; **74:** 58–65.
2 Dusting GJ, Macdonald PS. Endogenous nitric oxide in cardiovascular disease and transplantation. *Ann Med* 1995; **27:** 395–406.
3 Kharitonov SA, Barnes PJ. Exhaled nitric oxide: a marker of airway inflammation? *Curr Opin Anaesth* 1996; **9:** 542–48.
4 Date H, Triantafillou AN, Trulock EP, Pohl MS, Cooper JD, Patterson GA. Inhaled nitric oxide reduces human lung allograft dysfunction. *J Thorac Cardiovasc Surg* 1996; **111:** 913–19.
5 Marczin N, Riedel B, Royston D, Yacoub M. Intravenous nitrite vasodilators and exhaled nitric oxide. *Lancet* 1997; **349:** 1742.

Department of Cardiothoracic Surgery, National Heart and Lung Institute, Imperial College of Science Technology and Medicine, Harefield UB9 6JH, UK (M Yacoub)**; Department of Anaesthetics, Harefield Hospital, Harefield; and Department of Histochemistry, Royal Postgraduate Medical School, Hammersmith Hospital, London**

Penile rigidity in erectile dysfunction treated with alprostadil

Ermanno Greco, Paolo Polonio-Balbi

Clinical efficacy of transurethral alprostadil has been tested by evaluating the penile response with systems such as the Erection Assessment Scale, although several studies indicate that penile rigidity assessed by an objective method is the only valid way to test the efficacy of any treatment. We evaluated the efficacy of transurethral alprostadil by assessing both axial and radial rigidity.

123 patients, aged 33–77 years were studied. Alprostadil was inserted into the distal urethra with a drug delivery system (MUSE, Vivus, CA, USA) according to the instructions of the manufacturer. After administration of the drug, a colour-doppler device detected the passage of the drug into the cavernous bodies through the increase of the blood flow in the penile arteries. Axial rigidity was assessed by penile buckling test—positive when a downward axially-directed strength of 1 kg did not buckle the penis. Radial rigidity was assessed by an electronic rigidometer RIGICOMPT (Androsystems, Rome, Italy), with a pressure transducer in contact with the side wall of the penis, to measure its hardening.[4] Rigidity was judged to be complete when pressure was more than 75 mm Hg after visual erotic stimulation. Almost all the patients (n=117) had previously been on intracavernous insections; six patients had not had any treatment. Ten patients received the 250 μg, the rest 500 μg dosage as the first dose.

All patients had an improvement of arterial inflow which was detected by the doppler proving the passage of the drug into the corpora cavernosa. There was complete rigidity in 11 men; and a full but not a lasting erection (1–2 min) in 16. There was an increase in volume, up to 114%, in almost all patients, but not many had a real and lasting hardness. There seems to be no correlation between volume increase and hardness. Five patients wished to try the system at home, two of them got good results, the rest wished to stay on intracavernous injections.

1 Padma-Nathan H, Hellstrom WJG, Kaiser FE, et al. Treatment of men with erectile dysfunction with transurethral alprostadil. *N Engl J Med* 1997; **336:** 1–7.
2 Virag R, Lajugie J, Virag H. Continuous monitoring of penile rigidity during the evaluation of impotence. In: Proceedings of the first world meeting on impotence. *N Engl J Med* 1997; **336:** 122.
3 Goldstein I, Auerbach S, Padma-Nathan H, Rafjer J, Nelson L, Albrecht D. Evaluation of penile rigidity by axial loading force during in-office dose titration and alprostadil alfadex in patients with erectile dysfunction. *Int J Impot Res* Special Issue: VII world meeting on impotence. 1996; **8:** 205 (P88).
4 Virag R, Virag H, Lajugie J. A new device for measuring penile rigidity. *Urology* 1985; **25:** 80–81.

Center for Impotence and Fertility, Viale Liegi 6, 00198 Rome, Italy (E Greco)