- broiler chickens. *Aust Vet J* 1986; 63: 377-378.
5. Yung AP, Grayson ML. Psittacosis — a review of 135 cases. *Med J Aust* 1988; 148: 228-233.
 6. King K. Histoplasmosis in Australia. *Med J Aust* 1982; 2: 550-551.
 7. Reed CE, Sosman A, Babee RA. Pigeon-breeders' lung. *JAMA* 1965; 193: 81-85.
 8. Korn DS, Florman AL, Gribetz I. Recurrent pneumonitis with hypersensitivity to hen litter. *JAMA* 1968; 205: 114-115.
 9. Christiansen LT, Schmidt CD, Robbins L. Pigeon breeders' disease — a prevalence study and review. *Clin Allergy* 1975; 5: 417-436.
 10. Bar-Sela S, Teichtahl IH, Lutsky I. Occupational asthma in poultry workers. *J Allergy Clin Immunol* 1984; 73: 271-275.
 11. Lutsky I, Teichtahl H, Bar-Sela S. Occupational asthma due to poultry mites. *J Allergy Clin Immunol* 1984; 73: 56-60.
 12. Ferris BG. Epidemiology standardization project. *Am Rev Respir Dis* 1978; 118(suppl 11): 1-120.
 13. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximum expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 1983; 127: 725-734.
 14. Dixon WJ, ed. BMDP statistical software. Berkeley: University of California Press, 1983.
 15. Chronic bronchitis, asthma and pulmonary emphysema. A statement by the committee on diagnostic standards for non-tuberculous respiratory diseases. *Am Rev Respir Dis* 1962; 85: 762.
 16. Lazarus R. Determination of reference ranges for pulmonary function: methodological issues in the investigation of factors influencing respiratory health in Victoria power industry workmen [Master of Medicine thesis]. Melbourne: University of Melbourne, 1984.
 17. Leigh J, Wiles AM, Glick M. Total population study of factors affecting chronic bronchitis prevalence in the coal mining industry of New South Wales, Australia. *Br J Ind Med* 1986; 43: 263-271.
 18. Australian Bureau of Statistics. Smoking and asthma, South Australia. Adelaide: ABS, 1987. (Catalogue no. 4306.4.)
 19. Christie D, Gordon I, Robinson K. Smoking in an industrial population: an analysis by birth cohort. *Med J Aust* 1986; 145: 11-14.
 20. Bongers P, Houthuijs D, Remijn B, et al. Lung function and respiratory symptoms in pig farmers. *Br J Ind Med* 1987; 44: 819-823.
 21. Donham KJ, Zavala DC, Merchant JA. Respiratory symptoms and lung function among workers in swine confinement buildings: a cross-sectional epidemiological study. *Arch Environ Health* 1984; 39: 96-101.
 22. Holman CDJ, Psaila-Savona P, Roberts M, McNulty JC. Determinants of chronic bronchitis and lung dysfunction in Western Australian gold miners. *Br J Ind Med* 1987; 44: 810-818.
 23. Rylander R. Ongoing dusts and lung reactions — exposure characteristic and mechanisms for disease. *Scand J Work Environ Health* 1985; 11: 199-206.
 24. Elman AJ, Tebo T, Fink JN, Barboriale JJ. Reactions of poultry farmers against chicken antigens. *Arch Environ Health* 1968; 17: 98-100.

(Received June 15; accepted December 13, 1989)

Could preventive intranasal interferon lower the morbidity in children prone to respiratory illness?

Robert M Douglas, Brian Moore, Helen B Miles and Carole B Pinnock

ABSTRACT Recent studies have demonstrated that rhinovirus infections can be prevented in the family setting through use of intranasal interferon sprays which are commenced when another family member develops a cold. One hundred and twenty-seven children aged 4-9 years who had been hospitalized during their first year of life for severe infections caused by respiratory syncytial virus were studied virologically and epidemiologically during a seven-month period which included the winter months. The hypothesis was that a significant part of their respiratory morbidity would be preventable by a contact prophylaxis approach using intranasal interferon. However, the findings suggest that a preventive approach of this kind would not substantially reduce the burden of respiratory illness in these children because: the target children themselves more often introduced illness into the family than did other household members; rhinovirus infections preventable by interferon were associated with little lower respiratory morbidity; and rhinoviruses were minor contributors to the total respiratory illness burden in these respiratory illness-prone children.

(*Med J Aust* 1990; 152: 524-528)

Interferon- α_2 has been effective in prophylaxis in the family setting in preventing acquisition of rhinovirus infections in adults.^{1,2} A dose of 5 million units instilled intranasally once a day for seven days after the index case in a family became ill was effective in preventing rhinovirus-associated colds but not in preventing illness associated with other respiratory viruses.¹ Higher doses of intranasal interferon are unlikely to be tolerated generally.^{3,4} This approach to prevention would be clinically useful if subgroups could be identified in whom substantial illness was precipitated by rhinovirus infections. Children who experience hospitalization for respiratory syncytial virus (RSV) infection of the lower respiratory tract in the first year of life are at particularly high risk of respiratory morbidity in subsequent years.⁵ These children tend to experience bronchial hyperactivity, clinical asthma and prolonged and repeated respiratory infections. It seemed that this easily defined, high-risk group of children could benefit from a preventive approach if it could be shown that a significant proportion of their morbidity were precipitated by rhinovirus infections and if it could also be shown that they often developed their infections after colds had been brought into the family by other family members. We undertook a descriptive study of 127 children who had all been hospitalized for RSV infection

of the lower respiratory tract in their first year of life, in an effort to explore the feasibility of preventing morbidity during the autumn, winter and early spring seasons.

Method

The study population comprised 127 children from among 165 children who had previously participated in a double-blind, randomized controlled trial of vitamin A supplementation, during which their mothers had maintained careful diaries on each child's respiratory symptomatology for the previous 12 months.⁶ (A \$75 financial incentive had been offered for seven months of diary keeping and they had been asked to call the study centre whenever the child developed respiratory symptomatology.) For the study children, nose, throat, cough, ear, breathing and fever symptoms were documented in the diary, and their severity graded by the mother. For each of the other household members, the daily record also indicated whether they were experiencing one or more respiratory symptoms.

Swabs for viral culture were collected when a study child who had been free of respiratory symptoms for three days developed two respiratory symptoms on one day or one respiratory symptom on two consecutive days. These were obtained from both nares and the pharynx and were stored in viral transport media and refrigerated overnight or transported on ice to the laboratories at the Institute of Medical and Veterinary Science, Adelaide, for viral studies. The laboratory procedures for virus identification have been described earlier.⁴

A "family episode" began when respiratory symptoms began in one or more family members and concluded either three days after the last member stopped having respiratory symptoms or three days after a seven-day hypothetical course of prophylactic medication (used as in the adult studies) would have been completed. All respiratory symptoms for the study children and days of symptoms for each family member were entered graphically on a family episode graph which was used to evaluate the potential usefulness of the contact prophylaxis model.¹

The protocol and consent forms for these procedures were developed in conformity with ethical guidelines developed by the Australian National Health and Medical Research Council and approved by the Ethics Committee of the Adelaide Children's Hospital.

Results

Study population characteristics

The average age of the study children was 6.4 years, with a range of 4 to 9 years, and two-thirds were male. On average each child had experienced 3.5 hospital stays in their lifetime for chest illness. Eighty-seven per cent were attending school or kindergarten; 47% had missed more than 16 days of school or kindergarten due to respiratory illness in the previous 12 months. Twenty-three per cent of the children were claimed usually to have a chesty cough, even

National Centre for Epidemiology and Population Health,
Australian National University, GPO Box 4, Canberra, ACT 2601.
Robert M Douglas, MA, MD; FRACP, FRACGP, Director.
Institute of Medical and Veterinary Science, Frome Road, Adelaide, SA 5000.
Brian Moore, BSc, Virologist.
University of Adelaide, Adelaide, SA 5001.
Helen B Miles, BSc, Research Assistant.
Carole B Pinnock, PhD, Research Fellow.
Reprints: Professor R M Douglas.

Right rhythm for life

RYTHMODAN

ANTIARRHYTHMIC

DISOPYRAMIDE

N.H.S. GENERAL BENEFIT 100 + 5 Repeats
Consult prescribing information before prescribing. In this publication, it appears on page...

ROUSSEL
Castle Hill, NSW 2154

RY90/JA1

RYTHMODAN

disopyramide

PRESCRIBING INFORMATION

Right rhythm for life

N.H.S. GENERAL BENEFIT
100 + 5 Repeats

ROUSSEL

Gladstone Road
Castle Hill, NSW 2154

PRESENTATION: Oral RYTHMODAN. RYTHMODAN 100 mg is available as opaque green/beige capsules marked "RY RL", each containing 100 mg disopyramide base.

RYTHMODAN 150 mg is available as opaque, white capsules printed "RY 150" in black.

RYTHMODAN Injection. RYTHMODAN is available as 5 ml ampoules, each ampoule containing 50 mg of disopyramide (as phosphate) (10 mg/ml) in packs of five ampoules.

ELECTROPHYSIOLOGY: RYTHMODAN prolongs the effective refractory period of the atria and the ventricles. The effective refractory period of the A-V node is either slightly shortened or unchanged. The relative refractory period of the His-Purkinje system is prolonged. A-V nodal conduction time is unchanged by RYTHMODAN. Conduction through the His-Purkinje system is unchanged or slightly delayed.

INDICATIONS: Oral RYTHMODAN is indicated in:

1. Maintenance of normal rhythm following conversion by RYTHMODAN injection, other parenteral drugs or electroconversion.
2. Prevention of arrhythmias after myocardial infarction.
3. Persistent ventricular extrasystoles.
4. Control of arrhythmias following the use of digitalis or similar glycosides.
5. Suppression of arrhythmias during surgical procedures, e.g. cardiac catheterization.
6. Prevention of paroxysmal supraventricular tachycardia.
7. Wolff-Parkinson-White syndrome.

RYTHMODAN injection is intended for intravenous use only and is indicated in the following conditions:

1. Control of ventricular arrhythmias after myocardial infarction.
2. Patients not responding to lignocaine or other i.v. treatment.
3. Other types of arrhythmias including supraventricular tachycardia, Wolff-Parkinson-White syndrome.
4. Conversion of supraventricular arrhythmias following myocardial infarction.
5. Control of ventricular extrasystoles.
6. Control of arrhythmias following digitalis or similar glycosides when RYTHMODAN cannot be administered orally, providing heart block is not present (see CONTRAINDICATIONS).

CONTRAINDICATIONS: RYTHMODAN is contraindicated in the presence of cardiogenic shock, pre-existing second- or third-degree A-V block (if no pacemaker is present), cardiomyopathy associated with cardiac insufficiency, untreated cardiac failure (see PRECAUTIONS), untreated glaucoma (see PRECAUTIONS) and known hypersensitivity to the drug.

PRECAUTIONS: Heart Failure/Hypotension. Disopyramide should not be used in patients with uncompensated or marginally compensated congestive heart failure or hypotension unless the congestive heart failure or hypotension is secondary to cardiac arrhythmia. Patients with a history of heart failure may be treated with disopyramide, but careful attention must be given to the maintenance of cardiac function, including optimal digitalization.

Cardiomyopathy. Disopyramide should not be administered to patients with cardiomyopathy and associated congestive heart failure unless the patient is adequately digitalized. Patients with myocarditis or other cardiomyopathy may develop significant hypotension in response to the usual dosage of disopyramide, probably due to cardio-depressant mechanisms. Therefore, a loading dose of disopyramide should not be given to such patients and initial dosage and subsequent dosage adjustments should be made under close supervision. (See DOSAGE & ADMINISTRATION.)

Heart Block. If first-degree heart block develops in a patient receiving disopyramide, the dosage should be reduced. If the block persists despite reduction of dosage, continuation of the drug must depend upon weighing the benefit being obtained against the risk of higher degrees of heart block. Development of second- or third-degree A-V block or unifascicular, bifascicular or trifascicular block requires discontinuation of disopyramide therapy unless the ventricular rate is adequately controlled by a temporary or implanted ventricular pacemaker.

QRS Widening. Although it is unusual, if significant widening (greater than 25%) of the QRS complex occurs during disopyramide administration, the drug should be discontinued.

Q-T Prolongation. As with other Type 1 antiarrhythmic drugs, prolongation of the Q-T interval (corrected) and worsening of the arrhythmia may occur. Patients who have evidenced prolongation of the Q-T interval in response to quinidine may be at particular risk if a Q-T prolongation of greater than 25% is observed and, if ectopy continues, the patient should be monitored closely, and consideration be given to discontinuing disopyramide.

Hypoglycaemia. In rare instances, significant lowering of blood glucose values has been reported during disopyramide administration.

Hypokalaemia. Antiarrhythmic drugs may be ineffective in patients with severe hypokalaemia. Therefore, a significant potassium deficit should be corrected before initiating disopyramide therapy.

Anticholinergic Activity. Because of its anticholinergic properties, disopyramide should not be used in patients with glaucoma or in patients with urinary retention unless adequate overriding measures are taken. In patients with a family history of glaucoma, intraocular pressure should be measured before initiating disopyramide therapy. Disopyramide should be used with special care in patients with myasthenia gravis since its anticholinergic properties could precipitate a myasthenic crisis in such patients.

Renal Impairment. More than 50% of disopyramide is excreted in the urine unchanged. Therefore RYTHMODAN dosage should be reduced in patients with impaired renal function (see DOSAGE & ADMINISTRATION). The electrocardiogram should be carefully monitored for prolongation of PR interval, evidence of QRS widening or other signs of overdosage (see OVERDOSAGE).

Hepatic Impairment. Hepatic impairment also causes an increase in the plasma half-life of disopyramide. Dosage should be reduced for patients with such impairment. The electrocardiogram should be carefully monitored for signs of overdosage (see OVERDOSAGE).

Use in Atrial Fibrillation or Flutter. Patients with these arrhythmias should be digitalized prior to disopyramide administration to ensure that possible drug-induced enhancement of A-V conduction does not result in an increase of ventricular rate beyond physiologically acceptable limits.

Drug Interactions. Whilst no specific drug interactions have been identified, the concomitant use of disopyramide with other Type 1 antiarrhythmic agents (such as quinidine or procainamide) and/or beta-blockers should be reserved for patients with life-threatening arrhythmias who are demonstrably unresponsive to single agent antiarrhythmic therapy. Such use may produce serious negative inotropic effects, or may excessively prolong conduction. This should be considered particularly in patients with any degree of cardiac decompensation or those with a prior history thereof.

Use in Pregnancy. Animal studies have not demonstrated any teratogenic effect and have revealed only minimal evidence of impaired fertility and slightly lower weight in treated rats at the time of weaning. However, no controlled studies of disopyramide have been performed in pregnant women and experience with disopyramide during pregnancy is limited. Disopyramide has been reported to stimulate contractions of the pregnant uterus. Therefore, use of disopyramide in women of child-bearing potential requires that the benefits of therapy be weighed against its possible hazards to the mother and foetus.

ADVERSE REACTIONS: The most common adverse reactions are associated with the anticholinergic properties of the drug. They include dry mouth, blurred vision, urinary hesitancy, constipation. These adverse reactions are nearly always dose-related and may disappear with dosage reduction. Other adverse reactions occurring less frequently include gastrointestinal irritation, urticaria, skin rashes, nausea, dizziness, general fatigue, headache and malaise. Following intravenous administration a transient fall in blood pressure of about 20 mm Hg and excessive widening of the QRS Complex have been commonly reported. With intravenous administration the occurrence of side-effects, especially profuse sweating, was often associated with too rapid administration of the drug.

DOSAGE & ADMINISTRATION: Oral RYTHMODAN. The following regime is suggested as a guideline; however, an initial dose regime may need to be modified if the clinical status of the patient changes. Recommended dose in adults is 300-800 mg daily in divided doses and should be adjusted according to the response of the patient. (Doses in excess of 1 g daily have been given to some patients.) Most patients respond to 100 mg 6 hourly. When treating arrhythmia by electroconversion it is advisable to start RYTHMODAN one to two days prior to the applied electric shock. During this period sinus rhythm may be achieved. In patients with myocardial infarction, administration of RYTHMODAN should be started as soon as oral therapy is practicable. Control of arrhythmia in some patients may be obtained within eight hours of oral administration.

Dosage in Renal Impairment. For patients with severe renal insufficiency (creatinine clearance < 40 ml/min) the recommended dosage regime is a 200 mg loading dose followed by 100 mg maintenance dose given approximately every half-life (t_{1/2}). See table below for relationship between creatinine clearance, half-life and the maintenance dosage interval.

Creatinine Clearance (ml/min)	1-5	5-15	15-40
Disopyramide t _{1/2} (hr)	37-26	26-15	15-7
Approximate maintenance dosing interval	q30hr	q20hr	q10hr

RYTHMODAN Injection. As adverse reactions are frequently associated with too rapid i.v. administration, the drug should be injected slowly over a period of 10-15 minutes. The recommended dosage can be given by two different regimes:

1. An initial intravenous injection of 2 mg/kg given slowly over 10-15 minutes until the arrhythmia is abolished or up to a maximum of 150 mg. Repeat if conversion is unsuccessful but arrhythmia recurs. Another slow, direct intravenous injection may be given cautiously, preferably under ECG control. N.B. Total i.v. dosage should not exceed 300 mg during the first hour.

2. An initial injection as in 1, followed by an infusion of 20-30 mg/hr (or 0.4 mg/kg/hr) up to a maximum of 800 mg daily. This could be used for patients in the Coronary Care Unit who have serious arrhythmias and for whom oral maintenance therapy is impracticable. The intravenous infusion is prepared by adding 200 mg RYTHMODAN to a 500 ml bottle of intravenous fluid (see Compatibility section). Using this infusion a drip rate of 1 ml/kg/hr will deliver 0.4 mg/kg/hr. There may be occasions when the clinician wishes to use more than 800 mg daily. He must then weigh the possible increases in therapeutic efficacy against the probable side-effects. The patient should be under continuous ECG control. Patients receiving intravenous RYTHMODAN should have their blood pressure and ECG closely monitored on a continuous basis and should be transferred to oral therapy, if appropriate, as soon as is practical.

Transfer to oral maintenance therapy from either i.v. injection or infusion is accomplished by giving 200 mg orally, immediately on cessation of i.v. administration, followed by 200 mg 8 hourly for 24 hours; subsequently maintenance is often achieved by a total daily dosage of 400-600 mg. Total i.v. and oral dosage should not exceed 800 mg in 24 hours.

Paediatric Use. Not recommended for use in children as the safety and efficacy in this age group have not been established.

COMPATIBILITY. RYTHMODAN injection should not be physically premixed with other drugs but should be administered separately in accordance with the recommended route of administration and dosage schedule.

RYTHMODAN injection is physically compatible with the following:

- Sodium Chloride Injection B.P.
- Dextrose Injection B.P.
- Compound Sodium Chloride Injection B.P.C.
- Compound Sodium Lactate Injection B.P.

Stability studies have shown that RYTHMODAN remains active in these infusion fluids for a period of at least 10 days.

N.B. Autoclaving of such admixture is not recommended because of the risk of breakdown of active principle.

OVERDOSAGE: Clinical Features. Massive fatal overdosage has been reported with coma, respiratory depression and abnormalities of cardiac rhythm. No specific antidote for disopyramide has been identified; treatment of overdosage should be symptomatic. Based on animal studies toxic serum levels of disopyramide might be expected to produce excessive widening of the QRS complex, worsening of congestive heart failure, hypotension, varying kinds of degrees of conduction disturbance, bradycardia leading to asystole and paradoxical ventricular fibrillation may be seen. Obvious anticholinergic effects might also be observed.

Management. In treating overdosage the drug should be discontinued immediately. The electrocardiogram should be monitored and supportive therapy with vasopressors, sympathomimetics, cardiac glycosides and diuretics should be given as required. If progressive heart block develops, endocardial pacing should be considered. Electroconversion of arrhythmia may be considered in life-threatening conditions. Anticholinergic effects may be reversed with neostigmine or physostigmine. In vitro studies with human blood have demonstrated that dialysis may be effective.

STORAGE: Store below 30°C.

when they did not have a cold, 64.8% were claimed to wheeze whenever they got a cold and 27% wheezed occasionally with exercise. At birth 44.5% had experienced breathing difficulty and 28.9% had weighed less than 3000 g. All of the study children had been admitted to hospital during their first year of life, suffering from lower respiratory illness associated either with isolation of, or seroconversion to, respiratory syncytial virus. Fifteen per cent were taking regular medication for asthma. For 11 of the children the symptom diary showed a consistent pattern of symptomatology which was declared in the early months of the study by the investigators as "background" against which judgements about the categorization of other episodic symptoms were superimposed.

Potential use of medication

The families of the 127 children experienced a total of 683 separate family episodes of respiratory symptomatology. Each family episode was examined to ascertain whether the circumstances were such that the study child could have been treated with interferon in contact prophylaxis form, that is, was the family episode initiated by respiratory illness in some family member other than the study child and was the child eligible to use medication in prophylactic form? (As with our earlier adult study we required two clear weeks between the end of one and the beginning of another hypothetical course of medication.)

In 335 of the 683 family episodes, application of these criteria would have enabled the child to commence taking intranasal interferon. Thus, during the average surveillance period of 204 days, there would have been, on average, 2.6 courses of medication used by each child in the study. In 155 of these 335 theoretically "medicable" episodes, the study child actually developed respiratory symptomatology. That is, in 46.3% of the family episodes in which contact prophylaxis could have been used, a respiratory illness was available for "prevention" in the study child.

Five hundred and fourteen episodes of respiratory symptomatology were experienced by the study children, that is, an average of 4.0 episodes per child during the seven months of surveillance. For 313 of these episodes the child was the "index" case in a family episode, and for 201 episodes, the child was a "secondary" case. In 155 of these 201 episodes, the child could have been using interferon prophylaxis (in 46 cases, a full two weeks had not elapsed since a previous hypothetical "course"). Table 1 shows a comparison of the symptom profile of the 155 "medicable" episodes with the 359 which were "non-medicable". The dominant symptoms in both groups were nasal and cough, with surprisingly little new wheeze developing over and above the background level. The medicable episodes did not differ substantially from those which were non-medicable.

Viral findings

Viral cultures were collected from study children in 354 of the 514 episodes (68.9%). The main viruses grown were rhinovirus (14.1%) with parainfluenza viruses from a further 4% of cultures. Table 2 shows a comparison of culture results in the 155 episodes which were medicable with those 359 episodes that were not. Rhinoviruses were implicated less frequently in the medicable group (10.7% of 122 cultures compared with 15.9% of 232 cultures collected from children who were experiencing "non-medicable" episodes). A comparison of the symptom profiles of episodes caused by rhinovirus with those from which parainfluenza virus was grown, showed that the parainfluenza virus episodes lasted longer (12.7 days v. 10.4 days) and were more often characterized by wheeze (3.0 days per episode v. 1.1 days per episode) than the episodes associated with rhinovirus.

Preventive possibilities

For the entire study, the children were observed for an average of 204 days and of these days, respiratory symptoms occurred on 45.4 days. Of these, 8.4 symptom days per child occurred outside defined respiratory episodes, that is, they were either sporadic single symptom days or part of a semicontinuous background of respiratory

TABLE 1: Comparison of 155 "medicable" and 359 "non-medicable" episodes

Variables	Medicable episodes (n=155)	Non-medicable episodes (n=359)
Mean duration (days)	9.3	9.1
Mean days of nasal symptoms	6.8	5.9
Mean days of throat symptoms	1.9	2.2
Mean days of cough symptoms	5.2	5.9
Mean days of ear symptoms	0.5	0.4
Mean days of wheeze symptoms	0.9	1.1
Mean days of shortness of breath	0.4	0.3
Mean days of fever symptoms	0.6	0.5
Mean days of antibiotic consumption	1.8	1.5
Mean number of doctor visits	0.34	0.46

symptomatology against which decisions about episode onset had to be made in a small group of 11 children. There remained an average of 37.0 symptom days per child which occurred within clearly defined respiratory episodes. Of these, 23.4 symptom days on average for each child occurred within episodes in which the child was an index case for a family episode. Another 1.9 symptom days per child, although part of a secondary episode within the family episode, could not have been prevented by contact prophylaxis because the child would not have been eligible to use medication. There finally remained an average of 11.7 symptom days per child which were susceptible to prevention by the contact prophylaxis method. As discussed below we could not hope to reduce this burden by more than 20% (that is, an average of two to three days).

Discussion

The basis for a family contact prophylaxis approach is that considerable transmission of viral respiratory infection occurs in the family setting. In our earlier study of contact prophylaxis in adults, interferon- α_2 prevented rhinovirus-associated colds in those who used contact prophylaxis during family episodes.¹ This episodic use of intranasal spray was associated with acceptably low levels of nasal irritation. Efficacy in the prevention of "definite" episodes of illness was 86% if rhinovirus were isolated from the index case in a family. But efficacy was confined to family episodes in which rhinovirus was cultured either from the index case or from one or more of the secondary cases. The net benefit to those who used the active preparation was a 20% difference in respiratory symptom days.

The present study used identical virological laboratory procedures which were carried out by the same laboratory personnel as those used in the adult studies. Rhinovirus was grown in 10.7% of medicable episodes in the present study. The comparable percentage was 15.5% in the adult study. Thus a lesser net reduction in episodes in this population would be expected than that which we observed in the adult study because of the smaller contribution of rhinovirus. Accordingly, we do not have a basis for expecting a reduction of as much as a mean of 2.3 (20%) of the 11.7 days of respiratory symptomatology which are theoretically available for prevention. Thus, we could expect for 18.2 days of prophylactic dosing with interferon, a prevention of fewer than 2.3 days of respiratory symptoms per child during the average 204 days of surveillance to which each

TABLE 2: Comparison of viral culture results in "medicable" and "non-medicable" episodes

Viral culture	Medicable episodes (n=155)	Non-medicable episodes (n=359)
Rhinovirus	13 (10.7%)	37 (15.9%)
Parainfluenza virus	6 (4.9%)	8 (3.4%)
Respiratory syncytial virus	1 (0.8%)	1 (0.4%)
Adenovirus	2 (1.6%)	3 (1.3%)
Other viruses	5 (4.1%)	6 (2.6%)
Negative culture results	95 (77.8%)	177 (76.3%)
Culture not done	33	127

study child was submitted. In this study, wheeze was observed for an average of 1.1 days of every 10.4 days of rhinovirus episodes. So, within the maximum 2.3 days available for symptom reduction, we would not expect prevention of more than 0.24 days per child of wheezing throughout the six months of the study.

Viruses were cultured in only 22.2% of medicable and 23.8% of non-medicable episodes in this study. This viral isolation rate is comparable to the viral yield in the earlier adult study. We do not know the contribution of coronaviruses to the present cases as they were not assessed serologically, but our adult studies suggested that contact prophylaxis was ineffective in preventing coronavirus infections.

We conclude that the contact prophylaxis approach in these high-risk children does not offer theoretical benefits. Our observations show that these young school-age children are more often than not the initiators of respiratory episodes within their families and therefore at these times would be unable to make use of contact prophylaxis. Further, it would seem that while they experience

possibly preventable rhinovirus-associated illness, this infection is not associated with substantial lower respiratory symptomatology and that for them the cost of the intranasal medication would be relatively unlikely to be balanced by clinically appreciable benefits.

Acknowledgements

We acknowledge the important contribution of Dianne Markham, Lorraine Davies and Bernadette Roberts in maintaining regular liaison with parents, the role of the parents themselves in keeping the diaries and the research grant from Schering Ltd which enabled the study to be carried out.

References

1. Douglas RM, Moore BW, Miles HB, et al. Prophylactic efficacy of intranasal alpha-2 interferon against rhinovirus infections in the family setting. *N Engl J Med* 1986; 314: 65-70.
2. Hayden FG, Albrecht JK, Kaiser DL, et al. Prevention of natural colds by contact prophylaxis with intranasal alpha-2 interferon. *N Engl J Med* 1986; 151: 71-75.
3. Douglas RM, Albrecht JK, Miles HB, et al. Intranasal interferon alpha-2 prophylaxis of natural respiratory virus infection. *J Infect Dis* 1986; 151: 731-736.
4. Farr B, Gwaltney JM, Hayden FG. Prevention of natural rhinovirus infection by daily intranasal interferon. 13th International Congress of Chemotherapy, Vienna, Austria 1983; 60: 24-27.
5. Mok JY, Simpson H. Outcome for acute bronchitis, bronchiolitis and pneumonia in infancy. *Arch Dis Child* 1984; 59: 306-309.
6. Pincock CA, Douglas RM, Martin AJ, Badcock NR. Vitamin A status of children with a history of respiratory syncytial virus infection in infancy. *Aust Paediatr J* 1988; 24: 286-289.

(Received October 17; accepted December 18, 1989)

Treatment of idiopathic spasmodic torticollis with botulinum-A toxin: a pilot study of 19 patients

I T Lorentz, S Shanthi Subramaniam and C Yiannikas

ABSTRACT Nineteen patients with spasmodic torticollis, unresponsive to standard therapy, were administered local injections of botulinum-A toxin into the affected muscles. During an average follow-up period of 11.5 months, a more than 25% improvement was noted in 14 of 19 patients. All those with purely focal dystonia and 9 of 10 patients with a disease history of less than three years benefited from treatment. Side effects were insignificant and transient. Botulinum toxin is a very effective and safe method of treatment for spasmodic torticollis. (*Med J Aust* 1990; 152: 528-530)

The term "dystonia" was coined by Oppenheim in 1911¹ in describing six patients with alterations in muscle tone, sustained posturing and involuntary movements. Since then the definition of dystonia has undergone many modifications, and is now described as "a syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures".²

Dystonia is classified according to age of onset, aetiology (symptomatic or idiopathic) and distribution. Thus, there are focal, segmental and generalized dystonias. Where a single area is involved, such as the eye (blepharospasm), face (oromandibular dystonia), neck (torticollis), or vocal cords (spasmodic dysphonia) the condition is called focal dystonia.² The commonest form of focal dystonia is spasmodic torticollis (ST) with a suggested prevalence of three per 10 000.³ When two or more contiguous parts are involved in the disease process, such as the face and the neck, for example, it is called segmental dystonia, and generalized dystonia when one or both legs and the trunk are affected. Hemidystonia involving half the body usually indicates symptomatic dystonia, with abnormality in the basal ganglia.

Spasmodic torticollis was first described by François Rabelais, the French humanist, author and physician, in the 16th century. The mean age of presentation is 40 to 50 years, and the female to male ratio is 3:2.⁴ Various combinations of neck posture may occur, such as laterocollis, retrocollis and antecollis. The head may be tilted onto one shoulder, and one of the shoulders may be elevated and displaced anteriorly. Intermittent or continuous tremor or spasmodic

movement may occur. The severity of the abnormal postures and movements can be aggravated by stress and an activity such as walking, while improvement may be achieved by the patient touching the chin, face or the back of the head. This is the so-called *geste antagonistique*, quite characteristic of ST but lacking an adequate explanation at the present time. The involuntary movements cease during sleep. Pain can be very severe, intractable and disabling. The onset may be sudden or gradual, the condition usually progressing for a few years and then becoming stationary. Remissions occur in 15% of patients, usually in the first few years after the onset. Many patients are unable to work, and even such activities as driving a car, eating, reading or watching television may become difficult or impossible. The obvious neck deformity causes a constant embarrassment, and the patient's suffering is increased by the lack of understanding and the ineffective therapies available. Medical treatment and psychotherapy are usually unsuccessful.⁵⁻⁷ Surgical treatment may have adverse results,⁸ a significant morbidity and even a small mortality.⁹

Botulinum-A toxin, a neuroparalytic agent, has recently been used in the treatment of focal dystonias. It was pioneered for the treatment of strabismus by Dr Alan Scott¹⁰ and has been shown to be effective for the treatment of blepharospasm,¹¹⁻¹⁴ oromandibular dystonias,¹⁵ spasmodic torticollis,¹⁶⁻²⁰ spasmodic dysphonia²¹ and focal hand dystonias.²² Clostridium botulinum produces eight distinct neurotoxins, which cause widespread muscular paralysis, characteristic of the often fatal syndrome of botulism. When botulinum-A toxin is injected intramuscularly in minute quantities local denervation and muscle weakness occur, lasting for several weeks until the nerve endings regenerate. The toxin inhibits the release of acetylcholine, probably by interfering with calcium channels.²³

Over the past two years we have used botulinum-A toxin to treat over 75 patients suffering from ST. We report the results of a pilot study of the first 19 patients, who have been followed up for an average of 11.5 months.

Patients and methods

Nineteen patients (11 women and 8 men), aged from 30 to 76 years (average, 47.4), were entered in the study. The patients were referred to one of us (I T L) because of ST which was intractable to the usual medical and surgical measures. The duration of the torticollis before our treatment was from 9

Westmead Hospital, Hawkesbury Road, Westmead, NSW 2145.

I T Lorentz, MB BS, FRACP, FRCP(Lond.), FRCP(Edin.), Neurologist.

S Shanthi Subramaniam, BSc(Hons), Neurophysiology Technician.

C Yiannikas, MD, FRACP, Neurologist.

Reprints: Dr I Lorentz, 151 Hawkesbury Road, Westmead, NSW 2145.