

Chronic cough and gastroesophageal reflux

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We reviewed the charts of 20 patients with chronic cough of unknown cause who had been referred to a tertiary care respiratory centre from 1980 to 1984 to determine whether gastroesophageal reflux (GER) was a contributing factor. Fifteen of the patients complained of symptoms suggestive of GER: radiologic investigation of the upper gastrointestinal tract revealed hiatus hernia and GER in four, hiatus hernia alone in three, GER alone in two, decreased esophageal peristalsis in one and normal findings in four. Fiberoptic bronchoscopy in the four former smokers and one nonsmoker showed diffuse mucosal erythema. A chest x-ray film in one patient showed an infiltrate at the base of the right lung; transbronchial biopsy revealed vegetable material, which confirmed pulmonary aspiration. A 3-month course of medical antireflux treatment (dietary and lifestyle changes, elevation of the head of the bed and administration of cimetidine, antacid and metoclopramide) relieved the chronic cough in 14 of the 20 patients. Of the remaining patients one was lost to follow-up and five had GER confirmed by means of esophagoscopy, esophageal motility testing and long-term intraesophageal pH monitoring; four of the five patients underwent fundoplication and were asymptomatic 3 months after surgery. Antireflux therapy should be considered in patients with chronic cough when other causes have been ruled out, even if there are no GER symptoms. If the treatment fails, full investigation for GER is recommended; if GER is confirmed, surgery should be considered.

Revue sur dossiers de 20 malades, adressés pour toux chronique de cause inconnue à un centre de soins tertiaires pour maladies respiratoires de

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1980 à 1984, chez qui nous avons recherché le rôle possible d'un reflux gastro-oesophagien (RGO). Quinze de ces malades accusaient des symptômes évoquant un tel reflux; l'étude radiologique montre quatre cas de hernie hiatale avec RGO, trois cas de hernie seule, deux cas de RGO seul, un cas de diminution du péristaltisme oesophagien. Les quatre autres malades ont un transit oesophago-gastrique normal. Chez les quatre anciens grands fumeurs et chez un non-fumeur, la bronchoscopie avec guide de lumière décèle un érythème diffus de la muqueuse. La radiographie d'un malade démontre un infiltrat à la base du poumon droit; la biopsie transbronchique ramène des matières végétales témoins d'une fausse-route alimentaire. Chez 14 de ces 20 malades on arrive à soulager la toux chronique par une thérapeutique anti-reflux comprenant diététique, modification du genre de vie, élévation de la tête du lit, prise de cimetidine, d'un anti-acide et de métopramide. Des six restants, un malade est perdu de vue; chez les cinq autres on confirme la présence d'un RGO par l'oesophagoscopie, l'étude de la cinétique oesophagienne et la surveillance prolongée du pH intra-oesophagien. Les quatre sujets qui ont subi une fondoplicature sont asymptotiques au bout de 3 mois. Devant un tousseur chronique chez qui on a éliminé les autres causes, il faut penser à mettre en route un traitement anti-reflux même s'il ne présente aucun symptôme de RGO. Si ce traitement ne réussit pas, on recommande l'exploration complète à la recherche d'un RGO. La découverte de celui-ci doit alors faire penser à un traitement chirurgical.

Although the association between gastroesophageal reflux (GER) and bronchial asthma has been well established,¹⁻¹⁹ the role of GER in causing chronic cough has received little attention in the literature.²⁰⁻²² We reviewed the charts of 20 patients who had chronic cough of unknown cause to determine whether gastroesophageal reflux was a contributing factor.

Patients

We reviewed the charts of all patients referred to two physicians in a tertiary care regional chest clinic from 1980 to 1984 to identify those with chronic cough of unknown cause who continued to cough despite therapy. Twenty such patients were identified.

The mean duration of the cough was 4.3 years (extremes 3 months and 25 years). In 12 patients the cough occurred predominantly at night. Five patients reported that they produced small volumes of sputum, but none had hemoptysis. One patient had a history of rhinitis, five reported wheezing, especially at night, and only three reported dyspnea. Fifteen of the 20 patients complained of symptoms suggestive of GER; these included a sour taste in the mouth at night (in 6), morning laryngitis (in 6), heartburn (in 4), chest pain in the supine position (in 4) and choking at night (in 2). None of the patients had a history of sinusitis, cardiac disease, underlying neurologic disease, intake of excessive amounts of ethanol or recent upper respiratory tract infection. None had experienced night sweats, fever or weight loss. Eighteen of the 20 patients were nonsmokers; at presentation 4 had smoked but had stopped 6 months to 11 years (mean 7 years) before presentation. Nine patients were taking respiratory drugs: salbutamol (nine patients), long-acting orally administered theophylline preparations (two) and orally administered prednisone (one).

Clinical findings

Physical examination and routine blood work revealed no abnormalities. Chest x-ray films appeared normal in 17 patients. Of the abnormal films two showed calcified lesions consistent with previous histoplasmosis, and one revealed an infiltrate at the base of the right lung.

Spirometry results before and after inhalation of 200 μ g of salbutamol were normal in all patients. Inhalation challenge testing was done according to the method of Cockcroft and associates.²³ In all of the patients the forced expiratory volume in 1 second decreased by less than 20% after 16 mg/ml of histamine or methacholine had been inhaled for 2 minutes; these results indicated normal airway reactivity.

Fibreoptic bronchoscopy performed in the four former smokers and one nonsmoker revealed diffuse mucosal erythema, which indicated tracheobronchitis, but no other endobronchial abnormalities were found. The patient in whom the chest x-ray film revealed an infiltrate underwent transbronchial biopsy: the specimen contained vegetable matter, indicating that aspiration had occurred.

Fourteen of the 15 patients with GER symptoms underwent radiologic investigation of the upper gastrointestinal tract. The findings were normal in four and revealed hiatus hernia and GER

in four, hiatus hernia alone in three, GER alone in two and reduced peristalsis in the lower region of the esophagus in one. Aspiration of barium into the tracheobronchial tree was not observed.

Treatment

All of the patients were treated for 3 months with a standard antireflux regimen: avoidance of fatty foods, coffee, tea, cigarettes and alcohol; intake of small regular meals, with nothing to eat or drink for 3 hours before bed except for sips of fluid with medication; elevation of the head of the bed 15 to 20 cm; and drug therapy (cimetidine, 300 mg 4 times daily, or ranitidine, 150 mg twice daily, along with metoclopramide, 10 mg before meals, and an antacid, 30 ml at bedtime).

Response to treatment

Fourteen (70%) of the 20 patients stopped coughing after antireflux therapy; 3 subsequently stopped the therapy, and their cough promptly returned. The response did not differ between the patients with symptoms of GER and those without such symptoms. Of the six patients who continued to cough, one was lost to follow-up, and five underwent further investigation for GER.

Endoscopic examination of the upper gastrointestinal tract revealed erythema, erosions or ulceration consistent with esophagitis in all five patients. Esophageal motility studies revealed reduced tone of the gastroesophageal sphincter consistent with (but not in itself diagnostic of) GER. The results of the Bernstein acid perfusion test²⁴ were positive in two patients who had heartburn. Long-term ambulatory and nocturnal intraesophageal pH monitoring confirmed prolonged episodes of GER. Moreover, through the use of an event marker a clear relation was established between episodes of GER and bouts of coughing (Fig. 1).

Fundoplication was done in four of the five patients; the fifth patient, an elderly woman, declined surgery and has remained symptomatic. At follow-up 3 months after surgery the patients were free of cough.

Discussion

Between 36% and 42% of adults who present with chronic cough to tertiary care respiratory centres have evidence of airway hyperreactivity;^{20,21} additional clues, such as dyspnea and wheezing, that suggest a diagnosis of asthma may be absent.²⁵ Other common causes of chronic cough include postnasal drip (in 8% to 25% of patients),^{20,21} postnasal drip associated with airway hyperreactivity (in 18%)²⁰ and chronic bronchitis (in 12%),^{20,21} which is usually linked with cigarette

smoking. Less common causes of chronic cough include psychologic disturbance (in 6%),²¹ cardiac disease (in 2% to 3%),^{20,21} primary or secondary malignant disease (in 1% to 2%)^{20,21} and sarcoidosis (in 1%).²⁰

In studies that excluded well-recognized causes of chronic cough, between 4%²¹ and 10%²⁰ of patients were shown to have GER, and their cough disappeared with the use of antireflux therapy.^{20,21} The results of our study are consistent with these findings.

GER can cause coughing in many ways. In healthy subjects and patients with documented GER, aspiration of gastric juices into the tracheobronchial tree has been shown to occur at night;²⁶⁻²⁹ even on an intermittent basis this may result in chemical tracheobronchitis.^{30,31} Gastric irritation has been shown in cats to cause a vagally mediated increase in the secretion of tracheal mucus³² and thus may cause chronic productive cough. Vagally mediated reflexes originating from receptors in the middle region of the esophagus are known to cause bronchoconstriction³³⁻³⁷ and to increase bronchial responsiveness to methacholine^{38,39} and isocapnic hyperventilation with dry air.³⁹ Theophylline increases the amount of gastric acid secreted,^{40,41} reduces the tone of the gastroesophageal sphincter⁴¹⁻⁴³ and induces acid reflux and reflux-related symptoms.⁴² It has been suggested that increased respiratory efforts alone may induce GER,⁴⁴⁻⁴⁶ but incremental inspiratory-resistive loading failed to demonstrate GER in healthy subjects, in a healthy subject receiving theophylline infusion therapy and in patients with reflux esophagitis;⁴⁷ indeed, inspiratory efforts prevented GER or terminated an episode of GER that had been experimentally induced by means of esophageal distension.

Clinical signs of GER in a patient whose primary complaint is chronic cough include cough associated with the ingestion of food or cold liquids,³⁹ nocturnal cough,^{2,16,17,46} cough that is exacerbated rather than relieved by bronchodilator or steroid therapy⁴⁸ and cough that is associated with typical symptoms of GER: heartburn, acid regurgitation, morning hoarseness, dysphagia and choking.

Even if the evidence strongly suggests that respiratory symptoms are related to GER, other causes of chronic cough must be excluded. Airway hyperreactivity should be ruled out by means of challenge testing with histamine, methacholine, cold air or exercise; evidence of rhinitis, sinusitis and postnasal drip should be sought; and disease of the lung parenchyma and bronchi should be ruled out. In some patients a chest x-ray film is sufficient, and in others bronchoscopy may be indicated. In the latter, erythema of the segmental and subsegmental airways has been reported to be a sign of pulmonary acid aspiration.³¹

Once primary respiratory disease has been excluded a barium swallow should be performed to rule out conditions of the esophagus that may predispose to aspiration; these include achalasia, scleroderma, pharyngeal pouch, esophageal carcinoma, esophageal stricture and tracheoesophageal fistula. The need for further investigation or treatment can then be decided on an individual basis. We usually start treatment with the diet and lifestyle regimen described previously together with antacid therapy or combined antacid-alginate therapy. It is particularly important that the head of the bed be elevated⁴⁹ and that the patient have nothing to eat or drink for at least 3 hours before sleep and avoid tea, coffee and very cold carbonated beverages. Many patients become asymptomat-

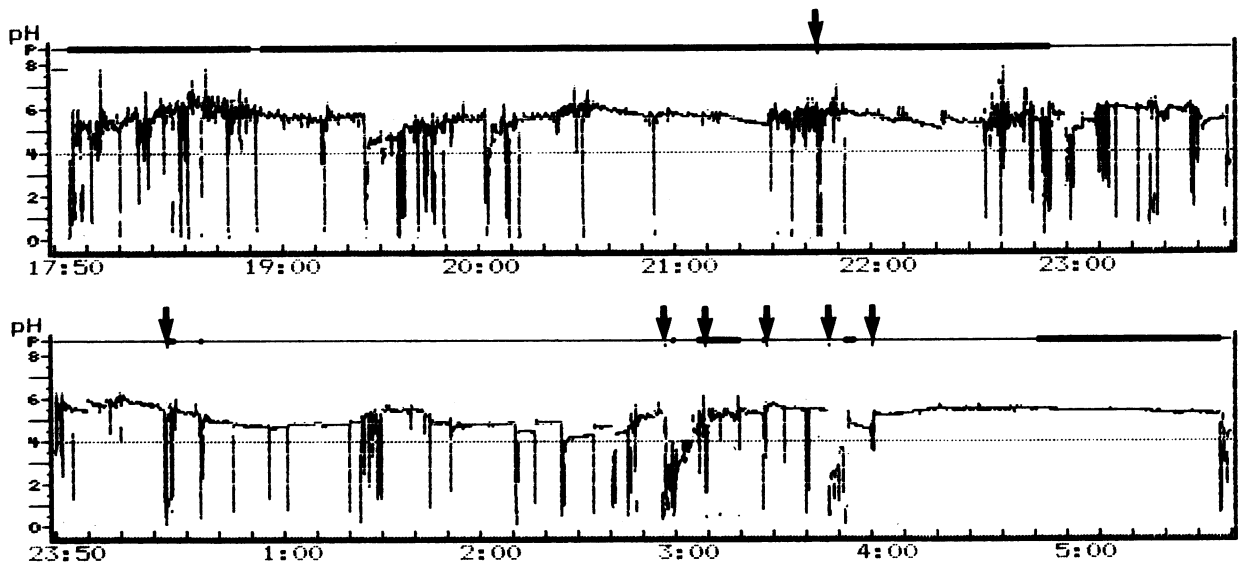


Fig. 1 — Esophageal pH tracing in patient with chronic night cough. Horizontal dotted line indicates esophageal pH of 4 (pH of less than 4 represents reflux). Arrows indicate occasions when patient pressed event marker to register coughing spells, all of which were related to gastroesophageal reflux. Horizontal position line (at top of each graph) represents periods when patient was supine (thin line) and upright (thick line).

ic; however, if the program fails, the combined use of an H₂-receptor antagonist and a peripheral dopamine antagonist (e.g., metoclopramide and domperidone) may help if delayed gastric emptying is suspected.

If symptoms persist endoscopy, long-term intraesophageal pH monitoring and esophageal motility testing should be done. The purpose of the esophageal motility testing is not to diagnose GER but, rather, to look for evidence of abnormal peristalsis and scleroderma that may affect the type of surgery performed. If radiologic and endoscopic findings are equivocal or negative, pH monitoring for 24 hours will not only detect GER but, more importantly, will allow the clinician to identify a consistent relation between GER and cough. In well-selected patients the results of surgery have been excellent.^{46,50}

Our study suggests that GER is an important cause of intractable chronic cough in patients seen at secondary and tertiary care centres and that in 90% of such patients the cough can be eliminated by means of appropriate medical or surgical anti-reflux therapy. Similarly impressive results in smaller groups of patients have been reported by other investigators,^{20,21} but as with all retrospective studies the results should be confirmed with randomized controlled studies.

References

1. Babb RR, Notarangelo J, Smith VS: Wheezing: a clue to gastroesophageal reflux. *Am J Gastroenterol* 1970; 53: 230-233
2. Berquist WE, Rachelefsky GS, Kadden M et al: Gastroesophageal reflux-associated recurrent pneumonia and chronic asthma in children. *Pediatrics* 1981; 68: 29-31
3. Christie DL, O'Grady LR, Mack DV: Incompetent lower esophageal sphincter and gastroesophageal reflux in recurrent acute pulmonary disease of infancy and childhood. *J Pediatr* 1978; 93: 23-27
4. Euler AR, Byrne WJ, Ament ME et al: Recurrent pulmonary disease in children: a complication of gastroesophageal reflux. *Pediatrics* 1979; 63: 47-51
5. Goodall RJ, Earis JE, Cooper DN et al: Relationship between asthma and gastro-oesophageal reflux. *Thorax* 1981; 36: 116-121
6. Kjellen G, Brundin A, Tibbling L et al: Oesophageal function in asthmatics. *Eur J Respir Dis* 1981; 62: 87-94
7. Kjellen G, Tibbling L, Wranne B: Effect of conservative treatment of oesophageal dysfunction on bronchial asthma. *Ibid*: 190-197
8. Klotz SD, Moeller RK: Hiatal hernia and intractable bronchial asthma. *Ann Allergy* 1971; 29: 325-328
9. Larrain A, Carrasco J, Galleguillos J et al: Reflux treatment improves lung function in patients with intrinsic asthma [abstr]. *Gastroenterology* 1981; 80: 1204
10. Martin ME, Grunstein MM, Larsen GL: The relationship of gastroesophageal reflux to nocturnal wheezing in children with asthma. *Ann Allergy* 1982; 49: 318-322
11. Mays EE: Intrinsic asthma in adults. *JAMA* 1976; 236: 2626-2628
12. Mitsuhashi M, Tomomasa T, Tokuyama K et al: The evaluation of gastroesophageal reflux symptoms in patients with bronchial asthma. *Ann Allergy* 1985; 54: 317-320
13. Overholt RH, Ashraf MM: Esophageal reflux as trigger in asthma. *NY State J Med* 1966; 1: 3030-3032
14. Overholt RH, Voorhees RJ: Esophageal reflux as a trigger in asthma. *Dis Chest* 1966; 49: 464-466
15. Perpina M, Ponce J, Marco V et al: The prevalence of asymptomatic gastroesophageal reflux in bronchial asthma and in non-asthmatic individuals. *Eur J Respir Dis* 1983; 64: 582-587
16. Perrin-Fayolle M, Bel A, Braillon G et al: Asthma and gastro-oesophageal reflux (GER). Results of surgical treatment of reflux in 50 patients. *Poumon Coeur* 1980; 36: 231-237
17. Perrin-Fayolle M, Bel A, Kofman J et al: Asthma and gastro-oesophageal reflux. Results of a survey over 150 cases. *Ibid*: 225-230
18. Shapiro GG, Christie DL: Gastroesophageal reflux in steroid-dependent asthmatic youths. *Pediatrics* 1979; 63: 207-212
19. Sontag SJ, Skorodin M, O'Connell S et al: Ambulatory 24 hour esophageal pH monitoring in patients with asthma [abstr]. *Gastroenterology* 1984; 86: 1261
20. Irwin RS, Corrao WM, Pratter MR: Chronic persistent cough in the adult: the spectrum and frequency of causes and successful outcome of specific therapy. *Am Rev Respir Dis* 1981; 123: 413-417
21. Poe RH, Israel RH, Utell MJ et al: Chronic cough: bronchoscopy or pulmonary function testing. *Am Rev Respir Dis* 1982; 126: 160-162
22. Stalberg M: Evaluating and treating intractable cough. *West J Med* 1985; 143: 223-228
23. Cockcroft DW, Killian DN, Mellon JJ et al: Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977; 7: 235-243
24. Bernstein LM, Baker LA: Clinical test for esophagitis. *Gastroenterology* 1958; 34: 760-781
25. Corrao WM, Braman SS, Irwin RS: Chronic cough as the sole manifestation of asthma. *N Engl J Med* 1979; 300: 633-637
26. Ghaed N, Stein MR: Assessment of a technique for scintigraphic monitoring of pulmonary aspiration of gastric contents in asthmatics with gastro-oesophageal reflux. *Ann Allergy* 1979; 42: 306-308
27. Huxley EJ, Viroslav J, Gray WR et al: Pharyngeal aspiration in normal adults and patients with depressed consciousness. *Am J Med* 1978; 64: 564-568
28. Boonyaprapa S, Alderson PO, Garfinkel DJ et al: Detection of pulmonary aspiration in infants and children with respiratory disease: concise communication. *J Nucl Med* 1980; 21: 314-318
29. Chernow B, Johnson LF, Janowitz WR et al: Pulmonary aspiration as a consequence of gastro-oesophageal reflux. *Dig Dis Sci* 1979; 24: 839-844
30. Wynne JW, Ramphal R, Hood CI: Tracheal mucosal damage after aspiration. A scanning electron microscope study. *Am Rev Respir Dis* 1981; 124: 728-732
31. Wolfe JE, Bone RC, Ruth WE: Diagnosis of gastric aspiration by fiberoptic bronchoscopy. *Chest* 1976; 70: 458-459
32. German VF, Corrales R, Ueki IF et al: Reflex stimulation of tracheal mucus gland secretion by gastric irritation in cats. *J Appl Physiol* 1982; 52: 1153-1155
33. Kjellen G, Tibbling L, Wranne B: Bronchial obstruction after oesophageal acid perfusion in asthmatics. *Clin Physiol* 1981; 1: 285-292
34. Mansfield LE, Hameister HH, Spaulding HS et al: The role of the vagus nerve in airway narrowing caused by intra-oesophageal hydrochloric acid provocation and esophageal distention. *Ann Allergy* 1981; 47: 431-434
35. Mansfield LE, Stein MR: Gastroesophageal reflux and asthma: a possible reflex mechanism. *Ann Allergy* 1978; 41: 224-226
36. Perpina M, Pellicer C, Marco V et al: The significance of the reflex bronchoconstriction provoked by gastroesophageal reflux in bronchial asthma. *Eur J Respir Dis* 1985; 66: 91-97
37. Spaulding HS, Mansfield LE, Stein MR et al: Further investigation of the association between gastroesophageal reflux and bronchoconstriction. *J Allergy Clin Immunol* 1982; 69: 516-521

38. Herve P, Denjean A, Jian R et al: Intraesophageal perfusion of acid increases the bronchomotor response to methacholine and isocapnic hyperventilation in asthmatic subjects. *Am Rev Respir Dis* 1986; 134: 986-989
39. Wilson NM, Dixon C, Silverman M: Increased bronchial responsiveness caused by the ingestion of ice. *Eur J Respir Dis* 1985; 66: 25-30
40. Foster LJ, Trudeau WL, Goldman AL: Bronchodilator effects on gastric acid secretion. *JAMA* 1979; 241: 2613-2615
41. Johannesson N, Andersson KE, Joellsson B et al: Relaxation of lower esophageal sphincter and stimulation of gastric secretion and diuresis by antiasthmatic xanthines. *Am Rev Respir Dis* 1985; 131: 26-31
42. Berquist WE, Rachelefsky GS, Kadden M et al: Effect of theophylline on gastroesophageal reflux in normal adults. *J Allergy Clin Immunol* 1981; 67: 407-411
43. Stein MR, Towner TG, Weber RW et al: The effect of theophylline on the lower esophageal sphincter pressure. *Ann Allergy* 1980; 45: 238-241
44. Boyle JT, Tuchman DN, Altschuler SM et al: Mechanisms for the association of gastroesophageal reflux and bronchospasm. *Am Rev Respir Dis* 1985; 131: S16-S20
45. Clemenccon GE, Osterman P: Hiatal hernia in bronchial asthma: the importance of concomitant pulmonary emphysema. *Gastroenterology* 1961; 95: 110-115
46. Pellegrini CA, DeMeester TR, Johnson LF et al: Gastroesophageal reflux and pulmonary aspiration: incidence, functional abnormality, and results of surgical therapy. *Surgery* 1979; 86: 110-119
47. Allen CJ, Waterfall WE: The effect of respiratory loading on the lower esophageal sphincter in normal subjects [abstr]. *Dig Dis Sci* 1984; 29: 567
48. Allen CJ, Newhouse MT: Gastroesophageal reflux and chronic respiratory disease. *Am Rev Respir Dis* 1984; 129: 645-647
49. Johnson LF, DeMeester TR: Evaluation of the elevation of the head of the bed, bethanecol, and antacid foam tablets on gastroesophageal reflux. *Dig Dis Sci* 1981; 26: 673-680
50. Henderson RD, Woolfe CR: Aspiration and gastroesophageal reflux. *Can J Surg* 1978; 21: 352-354

Meetings

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June 14-16, 1989: XXIV Canadian Congress of Neurological Sciences
Westin Hotel, Ottawa
Secretariat, Canadian Congress of Neurological Sciences,
116C-1330 15 Ave. SW, Calgary, Alta. T3C 3N6;
(403) 229-9544

June 16-18, 1989: Toronto International Orthopaedic Update
Medical Sciences Building, University of Toronto
Continuing Medical Education, Faculty of Medicine,
Medical Sciences Building, University of Toronto,
Toronto, Ont. M5S 1A8; (416) 978-2718

June 18-21, 1989: Canada Safety Council 20th National Safety Conference
Winnipeg Convention Centre
Marie Juneau, director, National Services, Canada Safety Council, 1765 St. Laurent Blvd., Ottawa, Ont. K1G 3V4; (613) 521-6881

June 18-23, 1989: Canadian Society of Laboratory Technologists National Congress
Saint John Trade and Convention Centre
CSLT National Congress 1989, PO Box 1076, Saint John, NB E2L 4E6

June 20-22, 1989: 4th Canadian Congress of Rehabilitation
Constellation Hotel, Etobicoke, Ont.
Canadian Rehabilitation Council for the Disabled,
Congress Secretariat, 2110-1 Yonge St., Toronto, Ont. M5E 1E5; (416) 862-0340, FAX (416) 865-1851

June 21-25, 1989: 2nd Annual Update in Emergency Medicine
Chateau Montebello, Montebello, PQ
Continuing Medical Education, Faculty of Medicine,
Medical Sciences Building, University of Toronto,
Toronto, Ont. M5S 1A8; (416) 978-2718

June 26-28, 1989: Canadian Association of Physicists Annual Congress
University of Guelph, Guelph, Ont.
Mona L. Jento, executive secretary, Canadian

Association of Physicists, 903-151 Slater St., Ottawa, Ont. K1P 5H3; (613) 237-3392, FAX (613) 238-1677

July 16-22, 1989: Les jeux mondiaux de la médecine et Symposium de la médecine sportive
Collège Ahuntsic, Montréal
Annie Alberro, Service de formation continue,
Fédération des médecins omnipraticiens du Québec,
1100-1440, rue Ste-Catherine ouest, Montréal, PQ H3G 1R8; (514) 878-1911, ou 1-800-361-8499 pour les indicatifs 514, 819, 418 et 613

Aug. 23, 1989: Canadian Medical Protective Association Annual Meeting
Auberge des Gouverneurs, Quebec
Beverley Allen, Canadian Medical Protective Association, Carling Square, 560 Rochester St., Ottawa, Ont. K1S 5K7; (613) 236-2100

Sept. 22-24, 1989: Pharmacy Association of Nova Scotia and the Nova Scotia Pharmaceutical Society Annual General Meeting and Conference
Holiday Inn Dartmouth, Dartmouth, NS
Patrick King, PO Box 3214(S), 1526 Dresden Row, Halifax, NS B3J 3H5; (902) 422-9583

Oct. 6-8, 1989: Congrès de l'Association québécoise des pharmaciens propriétaires
Hotel Bonaventure, Montréal
Yvon Clement, 1031 rue St-Denis, Montréal, PQ H2X 3H9; (514) 842-0515

Oct. 19-21, 1989: Learning Disabilities Association of Canada 7th National Conference: Lighting the Way
Hotel Newfoundland, St. John's
Judy Davis, conference coordinator, 12 Colville St., St. John's, Nfld. A1E 3J8; (709) 739-0611 or (709) 579-7273

Oct. 25-28, 1989: Canadian Cardiovascular Society 42nd Annual Meeting and Scientific Sessions
Vancouver Trade and Convention Centre
Abstract deadline is Apr. 24, 1989.
Mrs. D. Lourenço, Office of the Secretariat, 401-360 Victoria Ave., Westmount, PQ H4V 2J9; (514) 482-3407