The plasma concentrations of arachidonic acid and linoleic acid (the precursors of the PGE_2 inflammatory prostaglandins[9]) changed little in either group. It is possible that some of the deterioration in some clinical measurements in the control group was due to an effect on the immune system of a diet high in saturated fat.

Further studies will be needed to resolve certain questions raised by our study. These incude the relative roles of EPA and a polyunsaturated-fat diet in producing benefit, the most effective dose of EPA, and the possible role of a diet high in saturated fat in exacerbating the disease process.

Correspondence should be addressed to J. M. K., Division of Rheumatology, Department of Medicine, Albany Medical College, Albany, NY 12208, USA.

REFERENCES

1 Panush RS, Carter RL, Katz P, Lowsari B, Longley S, Finnie S. Diet therapy for rheumatoid arthritis. *Arthritis Rheum* 1983, **26:** 462–69.
2 Prickett JD, Robinson DR, Steinberg AD. Dietary enrichment with polyunsaturated fatty acid eicosapentaenoic acid prevents proteinuria and prolongs survival in NZAxNZW F_1 mice *J Clin Invest* 1981; **68:** 556–59.
3 Zurier RB. Prostaglandins, immune responses, and murine lupus *Arthritis Rheum* 1982, **25:** 804–09.
4. Karmali RA, Hanrahan R, Volkman A, Smith N. Prostaglandins and essential fatty acids in regulation of autoimmunity and development of antibodies to DNA in NZB×NZW F_1 mice. *Prog Lipid Res* 1981; **20:** 655–61.
5. Kunkel SL, Fantone JC, Ward PA, Zurier RB. Modulation of inflammatory reactions by prostaglandins *Prog Lipid Res* 1981; **20:** 633–40.
6. Bragdon JH, Karmen A. Effect of ingested fat on fatty acid composition of serum lipoproteins. *J Lipid Res* 1961, **2:** 400–02
7. Fischer S, Weber PC. Prostaglandin I_3 is formed in vivo in man after dietary eicosapentaenoic acid. *Nature* 1984; **307:** 165–68.
8. Seyberth HW, Oelz O, Kennedy T, et al. Increased arachidonate in lipids after administration to man: effects on prostaglandin biosynthesis. *Clin Pharm Ther* 1975; **18:** 521–29.
9. Bergstrom S, Danielsson H, Klenberg D, Samuelsson B. The enzymatic conversion of essential fatty acids into prostaglandins. *J Biol Chem* 1964; **239:** 4006–09.
10. Meade CJ, Mertin J. Fatty acids and immunity. *Adv Lipid Res* 1978; **16:** 127–65.
11 Mahoney EM, Scott WA, Landsberger FR, Hamill AL, Cohn ZA. Influence of fatty acyl substitution on the composition and function of macrophage membranes. *J Biol Chem* 1980; **225:** 4910–17.
12 American Rheumatism Association. Criteria for determination of progression of rheumatoid arthritis and of functional capacity of patients with the disease. Primer on the rheumatic diseases. *JAMA* 1973; **224** (suppl): 140.
13. Zurier RB, Sayadoff DM, Torrey SB, Rothfield NF. Prostaglandin E_1 treatment of NZB/NZW mice. I Prolonged survival of female mice. *Arthritis Rheum* 1977; **20:** 723–28.
14. Kunkel SL, Ogawa H, Ward PA, Zurier RB. Suppression of chronic inflammation by evening primrose oil. *Prog Lipid Res* 1981; **20:** 885–88.
15 Fernandez G, Yunis EJ, Good RA. Influence of diet on survival in mice. *Proc Natl Acad Sci USA* 1976; **73:** 1279–83.
16. Fernandez G, Friend P, Yunis EJ, Good RA. Influence of dietary restrictions on immunologic function and renal disease in NZBxNZW F_1 mice. *Proc Natl Acad Sci USA* 1978; **75:** 1500–09.

USE OF ETHER IN LIFE-THREATENING ACUTE SEVERE ASTHMA

C. E. ROBERTSON D. STEEDMAN
C. J. SINCLAIR D. BROWN
N. MALCOLM-SMITH

Department of Accident and Emergency Medicine and Department of Anaesthetics, Royal Infirmary, Edinburgh

Summary Two patients with acute severe asthma who had failed to improve with conventional treatment, mechanical ventilation, and halothane showed prompt bronchodilator response following administration of diethyl ether by inhalation. Airway pressures fell, and there was a dramatic improvement in blood gas analysis and clinical condition.

Case-reports

Case 1

A 16-year-old boy presented moribund to the accident and emergency department. He had a 4–5 year history of asthma but had never previously required hospital admission. His sole medication was salbutamol from an inhaler taken as necessary. The history preceding admission was of increasing dyspnoea over the previous half hour. On examination he was moribund, deeply cyanosed, and unresponsive to painful stimuli; a few feeble respiratory efforts were visible. He was intubated and ventilated with 100% oxygen. An electrocardiogram showed a sinus tachycardia with a rate of 130/min. A radial arterial line was inserted for arterial blood gas analysis. He was given 500 mg hydrocortisone through an intravenous line, together with a slow injection of 250 mg aminophylline. Salbutamol to a total of 3 mg was given through the endotracheal tube, and 0·3 ml adrenaline 1:1000 was administered subcutaneously. Arterial blood gas analysis on arrival was H^+ 205 nmol/l, pCO_2 16·2 kPa, bicarbonate 14·5 mmol/l, pO_2 4·1 kPa. 40 ml 8·4% sodium bicarbonate was slowly administered over the next 15 min, and ventilation was continued. There was no improvement in his condition. Chest X-ray showed hyperinflated lung fields but no evidence of pneumothorax. Inflation pressures were greater than 80 cm water. In view of his lack of response, 2% halothane was added to the oxygen through a mark II Fluotec vaporiser, and ventilation was continued. There was no improvement in his condition, and repeat arterial blood gas analysis revealed a deterioration, with H^+ 173 nmol/l, pCO_2 24·7 kPa, bicarbonate 26 mmol/l, pO_2 26 kPa. Halothane was discontinued and diethyl ether was administered by inhalation using a Mapleson type A circuit (approximate inspired concentration 15–20%). Before this the inflation pressures had continued to be greater than 80 cm water. Within 10 min of the administration of ether the inspiratory airway pressure had fallen to 20–30 cm water, with a striking improvement in bronchospasm on auscultation of the chest. Arterial blood gas analysis after a further 15 min showed H^+ 164 nmol/l, pCO_2 20·2 kPa, bicarbonate 23 mmol/l, pO_2 48 kPa. He required intubation and assisted ventilation for 3 h, and after extubation he was self-ventilating and breathing air. Blood gas analysis was normal. He was discharged from intensive care after 12 h with no evidence of hypoxic brain damage.

Case 2

A 48-year-old woman who had had asthma since childhood was admitted to the accident and emergency department with a 24 h history of increasing dyspnoea and wheeze. While in the ambulance her dyspnoea increased and she lost consciousness. Her regular medications included terbutaline and beclomethasone by inhaler and theophylline/ephedrine tablets. In the past she had required courses of oral steroids for control of her asthma, and she took glibenclamide for maturity-onset diabetes. On examination she was deeply cyanosed, with dilated pupils and a sinus bradycardia of 40/min. She was making minimal respiratory efforts. She was intubated and ventilated with 100% oxygen. Initial blood gases showed H^+ 131 nmol/l, pCO_2 15·6 kPa, bicarbonate 22 mmol/l, pO_2 18·1 kPa. She was given 500 mg hydrocortisone intravenously, salbutamol through the endotracheal tube to a total of 3 mg, and 150 mg aminophylline by intravenous infusion over 10–15 min. Despite these measures ventilation was difficult, and inflation pressures of 70 cm water were required. Chest X-ray showed hyperinflated lung fields with no evidence of pneumothorax. She was given 1 ml of 1:1000 adrenaline intravenously over 5 min, and halothane was added to the inspired oxygen at a concentration of 2%. Her clinical condition deteriorated slightly, the ECG monitor showed first-degree heart block, and blood pressure fell from 125/85 mm Hg to 90 mm Hg systolic. Since there was no improvement in her ventilation, and her inflation pressures continued to be 65–75 cm water, ether was given by inhalation. The changes of first-degree heart block resolved completely, and her blood pressure returned to its previous level. Within 10 min of ether administration the inflation pressures fell to 30 cm water. Further arterial blood gases showed a striking improvement, H^+ 80 nmol/l, pCO_2 6·9 kPa, bicarbonate 16 mmol/l, pO_2 63·6 kPa. Over the next 12 h her clinical condition improved greatly. She was extubated and made a complete recovery with no evidence of hypoxic brain damage.

Discussion

Conventional treatment with inhaled beta$_2$-agonists, aminophylline, and steroids has reduced the frequency of acute severe asthma attacks requiring mechanical ventilation. Slowly deteriorating patients who require intubation may show a significant improvement merely when the work of breathing is taken over by a ventilator, thus allowing the cumulative effect of various medications to improve the bronchospasm. Nevertheless there are a small number of patients who require immediate intubation, ventilation, and additional therapy as in the cases above.[1]

Experiments in animals and man have demonstrated that halothane has bronchodilator activity.[2,3] It relaxes smooth muscle and antagonises the bronchoconstrictor effects of both histamine and acetylcholine in tracheal muscle isolates. The specific mode of action has not been fully elucidated. An effect similar to beta-sympathomimetic agents has been postulated, although there is no evidence of increase in catecholamine levels.[4] In common with many other inhalational anaesthetics, halothane has a negative inotropic effect and predisposes to catecholamine-induced cardiac arrhythmias, which may be aggravated by concomitant acidosis and hypoxia.[5] In case 1 we were reluctant to increase the inspired concentration of halothane above 2% because of the risks of dangerous cardiac arrhythmias in the presence of severe respiratory acidosis. In case 2 electrocardiographic evidence of first-degree heart block accompanied the administration of halothane and was associated with a fall in systolic blood pressure. In both cases, the administration of ether resulted in prompt bronchodilatation with clinical and arterial blood gas improvement, and no adverse cardiac effects were observed.

In 1912 Trendelenberg observed a relaxation effect of diethyl ether on excised bronchial tissues obtained from animals.[6] In the 1930s two reports appeared of the use of diethyl ether in status asthmaticus.[7,8] In those cases the ether was mixed with olive oil in equal parts and administered per rectum. In 1952 Tausig et al showed an improved response when ether was administered by inhalation rather than rectally,[9] and in 1973 Mountford advocated its use intravenously.[10] In the past 20 years the use of ether for anaesthesia has declined dramatically, and halothane has been recommended for severe status asthmaticus.[5,11] Our two cases indicate that despite the potential risks of explosion and flammability, ether may also have a role in such life-threatening situations, particularly if conventional halothane administration has failed.

Correspondence should be addressed to C. E. R., Accident and Emergency Department, Royal Infirmary, Edinburgh EH3 9YW

REFERENCES

1. Scoggin CH, Sahn SA, Petty TL. Status asthmaticus: A nine-year experience *JAMA* 1977; **238:** 1158–62
2. Hickey RF, Graf PD, Nadel JA, et al. The effects of halothane and cyclopropane on total pulmonary resistance in the dog *Anesthesiology* 1969; **31:** 334–43
3. Shnider AM, Papper EM. Anesthesia for the asthmatic patient. *Anesthesiology* 1961; **22:** 886–92
4. Klide AM, Aviado DM. Mechanism for the reduction in pulmonary resistance induced by halothane *J Pharmacol Exp Ther* 1967; **158:** 28–35.
5. Schwartz SH. Treatment of status asthmaticus with halothane. *JAMA* 1984; **251:** 2688–89
6. Adriani J, Rovenstine EA. The effect of anesthetic drugs upon bronchi and bronchioles of excised lung tissue. *Anesthesiology* 1943; **4:** 253–62.
7. Kahn IS. Status asthmaticus *J Allergy* 1937; **8:** 158–61.
8. Maytum CK. Bronchial asthma. Relief of prolonged attack by colonic administration of ether. *Med Clin North Am* 1931; **15:** 201–10.
9. Tausig D, Papper EM, Barach AL. Contributions of anesthesiology to the management of patients with asthma. *NY State J Med* 1952, **52:** 1893–95
10. Mountford LO. Treatment of status asthmaticus *Br Med J* 1973; **1**: 47–48.
11. O'Rourke PP, Crone RK. Halothane in status asthmaticus *Crit Care Med* 1982; **10:** 341–43

INACTIVATION OF LYMPHADENOPATHY-ASSOCIATED VIRUS BY HEAT, GAMMA RAYS, AND ULTRAVIOLET LIGHT

B. SPIRE D. DORMONT
F. BARRÉ-SINOUSSI L. MONTAGNIER
J. C. CHERMANN

Unité d'Oncologie Virale, Institut Pasteur, 75015 Paris, France; and Division de Radiobiologie et Radioprotection, Centre de Recherches du Service de Santé des Armées, 92141 Clamart

Summary Lymphadenopathy associated virus is inactivated by heating at 56°C for 30 min, and is not inactivated by 2×10^5 rad gamma irradiation or 5×10^3 J/m^2 ultraviolet irradiation.

Introduction

AN earlier paper[1] described the effects of various chemical disinfectants on lymphadenopathy-associated virus (LAV), a possible cause of the acquired immunodeficiency syndrome (AIDS).[2] We report here the effects on the virus of heat, gamma rays, and ultraviolet light.

Methods

LAV was obtained by infection of T lymphocytes from a healthy adult.[1,2] The cells were stimulated with phytohaemagglutinin (PHA) for 3 days, infected with LAV (5000 cpm equivalent reverse transcriptase per 10^6 cells), and grown in RPMI 1640 medium supplemented with 10% fetal calf serum (FCS), 10% T cell growth factor (TCGF, Biotest), and anti-human-α-interferon and antibiotics (PSN Flobio).

Reverse Transcriptase Assay

LAV reverse transcriptase (RT) was measured in 0·1% Triton X 100 disrupted high speed pellets. The polymerase reaction mixture (50 μl) contained 50 mmol/l "tris" HCl pH 7·8, 20 mmol/l KCl, 1 mmol/l dithiotreitol, 5 mmol/l $MgCl_2$, 10 μCi tritiated thymidine triphosphate (30 Ci/mmol), and 0·1 OD/ml of poly-A-oligo-dT_{12-18} as template-primer.[3]

Viral Infectivity Assays

4×10^6 T cells from a healthy donor were stimulated with PHA (1/500) for 3 days, infected with treated or untreated LAV (5000 cpm

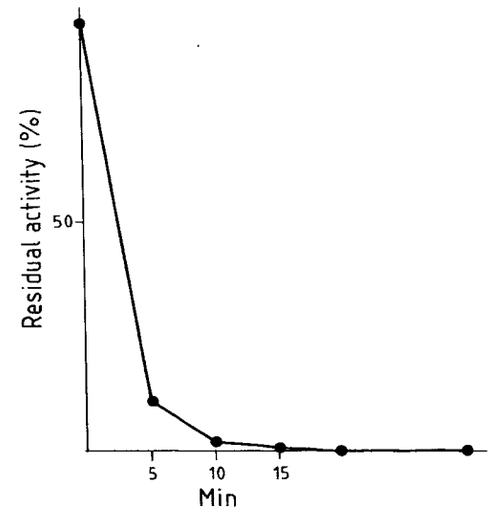

Fig 1—Inactivation of reverse transcriptase activity at 56°C.

10 μl of concentrated virus inactivated for different times at 56°C. Thermal inactivation was stopped by putting samples in ice.