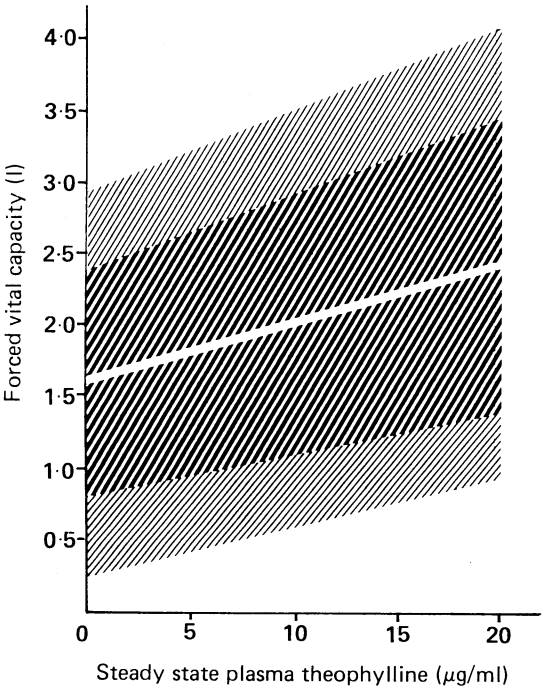

Absolute ventilatory response to increasing steady state theophylline concentrations in 56 patients with chronic bronchitis.[16] Heavily shaded area represents 1 SD around mean baseline value of 1·58 litres. Lighter shaded area extends to 2 SD. Clear line shows mean response with slope of 0·04 l μg⁻¹ ml. Reproduced with permission of Blackwell Scientific

of the lungs that cannot equilibrate with helium in the ordinary measurement of total lung capacity become accessible with the opening up of small airways.

Conclusions

All the evidence quoted above has passed a test of truth. This does not mean it is true, for we cannot rule out chance or honest error, but it does support my clinical conviction in prescribing theophylline. For the first 20 years of my career in respiratory medicine I considered theophylline to be a nuisance with no obvious effect except to make people feel sick. Ten years ago it became possible to use recent developments in clinical pharmacology to work out why some patients swore by the drug and to apply these advances to the benefit of some of the most severely handicapped and disadvantaged people in the population.

1 Altman DG. Statistics and ethics research. III. How large a sample? *Br Med J* 1980;**281**:1336-8.
2 Ward MJ. Clinical trials in acute severe asthma: are type II errors important? *Thorax* 1986;**41**:824-9.
3 Evans MV, Monie RDH, Crimmins J, Seaton A. Aminophylline salbutamol and combined intravenous infusions in acute severe asthma. *Br J Dis Chest* 1980;**74**:385-9.
4 Rees HA, Borthwick RC, Millar JS, Donald KW. Aminophylline in bronchial asthma. *Lancet* 1967;ii: 1167-9.
5 Rossing TH, Fanta CH, McFadden ER, *et al.* A controlled trial of the use of single versus combined drug therapy in the treatment of acute episodes of asthma. *Am Rev Respir Dis* 1981;**123**:190-4.
6 Vozeth S, Kewitz G, Perruchoud A, *et al.* Theophylline serum concentration and therapeutic effect in severe acute bronchial obstruction: the optimal use of intravenously administered aminophylline. *Am Rev Respir Dis* 1982;**125**: 181-4.
7 Barnes PJ, Greening AP, Neville L, Timmers J, Poole GW. Single-dose slow-release aminophylline at night prevents nocturnal asthma. *Lancet* 1982;i: 299-301.
8 Zwillich CW, Neagley SR, Cicutto L, White DP, Martin RW. Nocturnal asthma therapy. *Am Rev Respir Dis* 1989;**139**:470-4.
9 Greening AP, Baillie E, Gribbin HR, Pride NB. Sustained release oral aminophylline in patients with airflow obstruction. *Thorax* 1981;**36**:303-7.
10 Leitch AG, Morgan A, Ellis DA, Bell G, Haslett C, McHardy GJR. Effect of oral salbutamol and slow-release aminophylline on exercise tolerance in chronic bronchitis. *Thorax* 1981;**36**:787-9.
11 Mahler DA, Matthay RA, Snyder PE, Wells CK, Loke J. Sustained-release theophylline reduces dyspnea in non-reversible obstructive airways disease. *Am Rev Respir Dis* 1985;**131**:22-5.
11a Guyatt GH, Townsend M, Pugsley SO, *et al.* Bronchodilators in chronic air-flow limitation. *Am Rev Respir Dis* 1987;**135**:1069-74.
12 Dull WL, Alexander MR, Sadoul P, Woolson RF. The efficacy of isoproterenol inhalation for predicting the response to orally administered theophylline in chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1982;**126**:656-9.
13 Barclay J, Whiting B, Meredith PA, Addis GJ. Theophylline-salbutamol interaction; bronchodilator response to salbutamol at maximally effective plasma theophylline concentrations. *Br J Clin Pharmacol* 1981;**11**:203-8.
14 Barclay J, Whiting B, Addis GJ. The influence of theophylline on maximal response to salbutamol in severe chronic obstructive pulmonary disease. *Eur J Clin Pharmacol* 1982;**22**:389-93.
15 Taylor DR, Buick B, Kinney C, Lowry RC, McDevitt DG. The efficacy of orally administered theophylline, inhaled salbutamol, and a combination of the two as chronic therapy in the management of chronic bronchitis with reversible air-flow obstruction. *Am Rev Respir Dis* 1985;**131**:747-51.
16 Whiting B, Kelman AW, Struthers AD. Prediction of response to theophylline in chronic bronchitis. *Br J Clin Pharmacol* 1984;**17**:1-8.
17 Chrystyn H, Mulley BA, Peake MD. Dose response relation to oral theophylline in severe chronic obstructive airways disease. *Br Med J* 1988;**297**: 1506-10.

2 *Difficult drugs to use, few clinical indications*

I D A Johnston

University Hospital, Nottingham NG7 2UH
I D A Johnston, MD, *consultant physician*

Br Med J 1990;**300**:929-31

Theophyllines have been used for treating airflow obstruction for over 100 years.[1] In the United Kingdom alone 29 theophylline containing preparations are available, 16 of them being slow release. So why is their use still controversial?

Difficulties in using theophyllines

Theophyllines are undoubtedly difficult drugs to use properly. Firstly, effective bronchodilation without excessive side effects is achieved only within a narrow range of plasma concentrations. This therapeutic range is 10-20 mg/l, though some bronchodilatation occurs from 5 mg/l upwards.[1,2] Patients in general practice, however, tend to be given low doses, often with little or no therapeutic effect.[1]

Secondly, theophyllines often cause adverse effects. Minor or moderate effects such as nausea, headache, and jitteriness occur even at concentrations <10 mg/l and are common in the therapeutic range. Such effects may be reduced by introducing the drug slowly,[2,3] but they are severe enough to preclude maintenance treatment in a quarter of patients.[4] Toxicity, however, may be serious at concentrations >20 mg/l, when fits, arrhythmias, and death may occur.[5] These reactions are difficult to predict as they are not necessarily preceded by minor warning side effects and are not closely related to plasma concentrations.[3]

Thirdly, the dose of theophylline necessary to obtain therapeutic concentrations varies tremendously among patients—for example, from 450 to 2250 mg/day—because of wide individual variations in pharmacokinetics.[2-4] The clearance of theophylline is increased (concentrations will be lower) in children and smokers and decreased (concentrations will be higher) in older and obese patients and in heart failure, liver disease, and viral infections.[2,3] Many commonly prescribed drugs interact either to reduce plasma concentrations—for example, phenytoin, phenobarbitone—or, more seriously, to increase plasma concentrations, with potential toxicity—for example, cimetidine, erythromycin, oral contraceptives, ciprofloxacin, and allopurinol.[2,3] Therefore, to avoid toxicity and ensure drug effectiveness management must be guided by

plasma concentrations, especially at the start of treatment. With the right dose having been found and provided that the patient is clinically stable, concentrations may then need monitoring only annually, or six monthly in childhood.[1,3] Rapid analytical methods may become more widely available. Nevertheless, in general practice management by measuring plasma concentrations may be laborious and impracticable, and even in hospital only 10% of theophylline prescriptions were accompanied by a request for an estimation of plasma concentration.[5]

These problems with theophyllines would be worth overcoming if the drug was clearly the first choice in airways obstruction. Unfortunately the evidence suggests otherwise.

Difficulties in using theophylline

- Narrow therapeutic index
- Potentially toxic
- Plasma concentrations need to be monitored
- Other drugs offer comparable or better bronchodilatation

Not first line treatment but sometimes helpful in:

- Nocturnal asthma
- Poorly controlled severe chronic asthma
- Childhood asthma
- Acute severe asthma not responding to steroids, β agonists, and anticholinergics.

Asthma

Chronic stable asthma in adults

Theophyllines produce a dose related bronchodilatation comparable with that achieved with β agonists.[6,7] Despite differing pharmacological actions, however, the combination of theophyllines and β agonists does not act synergistically, and indeed the effect is usually less than additive.[6,7] Furthermore, maximum bronchodilatation can be achieved by inhaled β agonists irrespective of the theophylline concentration.[8] Set the comparable bronchodilator effects, but potential hazards, of theophyllines against the great advantages of inhaled β agonists in speed of action, convenience, and lack of side effects and the preferred bronchodilator should clearly be an inhaled β agonist, except in patients who prefer or who can only have oral treatment.

In persistent asthma the current trend is to use drugs that target the underlying airway inflammation. Regular inhaled steroids, sodium cromoglycate, and nedocromil are anti-inflammatory, have minimal toxicity, and are the preferred drugs for prophylactic treatment.

Theophyllines have been helpful in poorly controlled, more severe asthma[4] but are often disappointing when optimal doses of inhaled steroids and bronchodilators are being used.

Nocturnal asthma

Nocturnal wheeze and breathlessness, common in poorly controlled asthma, are often controlled by appropriate daytime doses of inhaled steroids. When nocturnal asthma remains troublesome, however, sustained release theophyllines can undoubtedly relieve symptoms and lessen the morning dip in lung function.[9,10] Theophyllines are probably more effective than long acting β agonists provided that therapeutic concentrations are attained, which requires doses of about 10 mg/kg.[9,10]

Acute severe asthma

Intravenous aminophylline in acute asthma provides no better bronchodilation than β agonists and little additional benefit when in combination with β agonists,[11,12] but it does produce more adverse effects.[12] Intravenous aminophylline should not be given to patients already taking theophyllines unless the concentration is measured as there is a serious risk of toxicity, bearing in mind that patients may increase their dose of oral theophyllines when their condition deteriorates. If absolutely necessary the usual bolus dose should be halved—that is, to only 3 mg/kg.

First line treatment should be nebulised β agonists (with ipratropium bromide if required) and steroids, with intravenous aminophylline being reserved for patients who deteriorate despite this treatment or who are desperately ill at presentation.[5,13]

Childhood asthma

The advantages of inhaled treatment and the problems of theophyllines apply also to children. Slow release theophyllines, often better tolerated in childhood, can, however, provide good prophylaxis between the ages of 2 and 5 years when inhaled treatment is difficult.[14] At other ages theophyllines are as effective in prophylaxis as sodium cromoglycate[15] but do not allow reduction of inhaled steroids.[16] Theophyllines also provide less protection than β agonists against asthma induced by exercise.[17] Furthermore, the use of theophylline is associated with poor concentration and irritabilty in children, with concern about longer term depression and anxiety.[18]

Chronic airflow obstruction

The use of theophyllines for chronic airflow obstruction is even more controversial than that for asthma,[1] partly because of the greater likelihood of toxicity in older patients with additional medical problems[19] but also because the clinical effects are disappointing.

Stable disease

In six placebo controlled randomised trials of oral theophylline in patients with chronic airflow obstruction with less than 20% reversibility, a marginal improvement in forced expiratory volume in one second was seen in only two.[20] The possible beneficial effects of theophylline on respiratory muscles have been debated but in none of these clinical studies was exercise performance significantly improved.[20] Even without objective benefit, it would clearly be valuable if theophyllines improved symptoms. In only two of the six studies, however, were symptoms convincingly improved.[20] In a longer term, though not double blind study, theophylline again improved the results of spirometry only marginally, but larger improvements were seen in less commonly measured indices such as the slow vital capacity. Nevertheless, even at the highest doses theophylline gave only a 20% increase in walking distance and modest reductions in dyspnoea.[21] β Agonists are more effective in such patients with poorly reversible disease,[19,22] and combined treatment is only marginally better than β agonists alone.[23]

In patients whose airflow obstruction is more reversible with β agonists theophyllines are, not surprisingly, more effective, and the combination of the two agents produces additional benefits.[24]

Acute exacerbations of disease

Intravenous aminophylline should not be routinely given as it gives no additional benefit over bronchodilators and steroids either in lung function or symptoms and results in more side effects.[25]

Summary

The narrow therapeutic index, potential toxicity, and need to monitor plasma concentrations make theophyllines difficult to use. Other drugs provide comparable or better bronchodilator and prophylactic efficacy.

In asthma theophyllines should be considered for chronic stable asthma when treatment with optimal doses of inhaled steroids and bronchodilators fails to provide adequate control; for nocturnal asthma; and for prophylaxis and relief of symptoms in children and adults when inhaled treatment cannot be given.

In general, theophyllines cannot be recommended for chronic airflow obstruction. A trial of theophylline is reasonable in individual patients whose symptoms remain troublesome despite a trial of steroids and optimal doses of inhaled bronchodilators.

1 Anonymous. Theophylline benefits and difficulties [Editorial.] *Lancet* 1983;ii: 607-8.
2 Bukowskyj M, Nakatsu K, Munt PW. Theophylline reassessed. *Ann Intern Med* 1984;**101**:63-73.
3 Weinberger M, Hendeles L. Use of theophylline for asthma. In: Clark TJH, Godfrey S, eds. *Asthma*. 2nd ed. London: Chapman and Hall, 1983:336-58.
4 Greening AP, Baillie E, Gribbin HR, Pride NB. Sustained release oral aminophylline in patients with airflow obstruction. *Thorax* 1981;**36**:303-7.
5 Woodcock AA, Johnson MA, Geddes DM. Theophylline prescribing, serum concentrations, and toxicity. *Lancet* 1983;ii:610-3.
6 Handslip PDJ, Dart AM, Davies BH. Intravenous salbutamol and aminophylline in asthma: a search for synergy. *Thorax* 1981;**36**:741-4.
7 Smith JA, Weber RW, Nelson HS. Theophylline and aerosolized terbutaline in the treatment of bronchial asthma. *Chest* 1980;**78**:816-8.
8 Klein JJ, Lefkowitz MS, Spector SL, Cherniack RM. Relationship between serum theophylline levels and pulmonary function before and after inhaled beta-agonists in "stable" asthmatics. *Am Rev Respir Dis* 1983;**127**:413-6.
9 Barnes PJ, Neville L, Greening AP, Timmers J, Poole GW. Single-dose slow-release aminophylline at night prevents nocturnal asthma. *Lancet* 1982;i: 299-301.
10 Zwillich CW, Neagley SR, Cicutto L, White DP, Martin RJ. Nocturnal asthma therapy. Inhaled bitolterol versus sustained release theophylline. *Am Rev Respir Dis* 1989;**139**:470-4.
11 Fanta CH, Rossing TH, McFadden ER. Treatment of acute asthma. *Am J Med* 1986;**80**:5-10.
12 Siegel D, Sheppard D, Gelb A, Weinberg PF. Aminophylline increases the toxicity but not the efficacy of an inhaled beta-adrenergic agonist in the treatment of acute exacerbations of asthma. *Am Rev Respir Dis* 1985;**132**: 283-6.
13 Anonymous. Acute asthma [Editorial]. *Lancet* 1986;i:131-3.
14 Milner AD. Bronchodilators in childhood asthma. In: Clark TJH, Cochrane GM, eds. *Bronchodilator therapy*. Auckland: Adis Press, 1984:93-111.
15 Edmunds AT, Carswell F, Robinson P, Hughes AO. Controlled trial of cromoglycate and slow-release aminophylline in perennial childhood asthma. *Br Med J* 1980;**281**:842.
16 Edmunds AT, McKenzie S, Baillie E, Tooley M, Godfrey S. A comparison of oral choline theophyllinate and beclomethasone in severe perennial asthma in children. *Br J Dis Chest* 1979;**73**:149-56.
17 Ellis EF. Inhibition of exercise-induced asthma by theophylline. *J Allergy Clin Immunol* 1984;**73**:690-2.
18 Furukawa CT, Duhamel TR, Weimer L, Shapiro GG, Pierson WE, Bierman CW. Cognitive and behavioral findings in children taking theophylline. *J Allergy Clin Immunol* 1988;**81**:83-8.
19 Cochrane GM. Slow release theophyllines and chronic bronchitis. *Br Med J* 1984;**289**:1643-4.
20 Hill NS. The use of theophylline in "irreversible" chronic obstructive pulmonary disease. *Arch Intern Med* 1988;**148**:2579-84.
21 Chrystyn H, Mulley BA, Peake MD. Dose response relation to oral theophylline in severe chronic obstructive airways disease. *Br Med J* 1988;**297**: 1506-10.
22 Dullinger D, Kronenberg R, Niewoehner DE. Efficacy of inhaled metaproterenol and orally-administered theophylline in patients with chronic airflow obstruction. *Chest* 1986;**89**:171-3.
23 Guyatt GH, Townsend M, Pugsley SO, *et al*. Bronchodilators in chronic airflow limitation. *Am Rev Respir Dis* 1987;**135**:1069-74.
24 Taylor DR, Buick B, Kinney C, Lowry RC, McDevitt DG. The efficacy of orally administered theophylline, inhaled salbutamol, and a combination of the two as chronic therapy in the management of chronic bronchitis with reversible air-flow obstruction. *Am Rev Respir Dis* 1985;**131**:747-51.
25 Rice KL, Leatherman JW, Duane PG. Aminophylline for acute exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987;**107**:305-9.

BOOKS RECEIVED

Acquired immune deficiency syndrome

AIDS and the Allied Health Professions. J W Hopp, E A Rogers. (Pp xxi+311; figs; £12.03 paperback.) Philadelphia: Davis, 1989. ISBN 0-8036-4677-1.

Clinical Practice of Gynecology. "AIDS in Gynecology." Ed N G Osborne. Series editor M S Baggish. (Pp viii+144; figs; $35.) New York: Elsevier, 1989. ISBN 0-444-01501-9.

Skin Manifestations of AIDS. N S Penneys. (Pp x+210; colour plates; £39.95.) London: Dunitz, 1989. ISBN 1-85317-013-5.

Alternative medicine

The Science and Art of Healing. R Twentyman. (Pp 315; figs; £19.95.) Edinburgh: Floris, 1989. ISBN 0-86315-095-0.

Bone

Bone Tumors: Clinical, Radiologic, and Pathologic Correlations. 2 vol set. J M Mirra, P Picci, R H Gold. (Pp xxxii+1831+indexes; figs and colour plates; £177.42.) Philadelphia: Lea and Febiger, 1989. ISBN 0-8121-1156-7.

Cardiology

Fetal, Neonatal, and Infant Cardiac Disease. J H Moller, W A Neal. (Pp xvii+1061; figs; £146.35). Connecticut: Appleton and Lange, 1989. Distributed by Prentice-Hall International. ISBN 0-8385-2575-X.

Health Care Technology Series. No 1. "Angioplasty and Other Percutaneous Interventional Techniques in the Treatment of Ischaemic Heart Disease. A literature review." M Rowe. (Pp iii+50; paperback, $A5 airmail postage and handling charge. 1989. Obtainable from Australian Institute of Health, Publications Section, PO Box 570, Canberra, ACT 2601, Australia. ISBN 0-642-14775-2.

Progress in Cardiology. Vol 2/2. Ed D P Zipes, D J Rowlands. (Pp xii+278; figs and colour plate; £28.03 paperback.) Philadelphia: Lea and Febiger, 1989. ISBN 0-8121-1190-7.

Thrombolysis in Cardiovascular Disease. Ed D G Julian, W Kubler, R M Norris, *et al*. (Pp xii+460; figs; price not stated.) New York: Dekker, 1989. ISBN 0-8247-8147-3.

Community medicine

Developing Friendships: Enabling People with Learning Difficulties to Make and Maintain Friends. A Richardson, J Ritchie. (Pp ii+101; £6.95 paperback.) London: Policy Studies Institute in association with Social and Community Planning Research, 1989. ISBN 0-85374-377-0.

Health Measurement Scales: a Practical Guide to Their Development and Use. D L Streiner, G R Norman. (Pp vii+175; figs; £25.) Oxford: Oxford University Press, 1989. ISBN 0-19-261773-7.

Ear, nose, and throat

Open Structure Rhinoplasty. C M Johnson Jr, D M Toriumi. (Pp xii+516; figs and colour plates; £210.) Philadelphia: Saunders, 1990. Distributed by Harcourt Brace Jovanovich. ISBN 0-7216-2158-9.

Endocrinology

Thyroid Function and Disease. G N Burrow, J H Oppenheimer, R Volpé. (Pp viii+335; figs; £46.50.) Philadelphia: Saunders, 1989. Distributed by Harcourt Brace Jovanovich. ISBN 0-7216-2190-2.

Gastroenterology

Clinical Research in Gastroenterology. 2. Ed S Matern. (Pp viii+98; figs; £22.50.) Dordrecht: Kluwer Academic, 1989. ISBN 0-7923-8906-9.

General medicine

Contemporary Internal Medicine. Vol 2. "Clinical Case Studies." Ed J Bowen, E L Mazzaferri. (Pp xvi+279; figs; $55.) New York: Plenum Medical, 1989. ISBN 0-306-43329-X.

General practice

Oxford General Practice Series. 17. "Family Problems." P R Williams. (Pp ix+108; figs; £12.50 paperback.) Oxford: Oxford University Press, 1989. ISBN 0-19-261604-8.

Geriatrics

Geriatric Medicine: Problems and Practice. M S J Pathy, P Finucane. (Pp xix+303; figs; £49.50.) London: Springer, 1989. ISBN 3-540-19525-4.

Health care issues

Community Involvement in Health Development: an Examination of the Critical Issues. P Oakley. (Pp viii+73; Sw frs 16 paperback.) Geneva: World Health Organisation, 1989. ISBN 92-4-156126-2.

Disabled Policy: America's Programs for the Handicapped—a Twentieth Century Fund Report. E D Berkowitz. (Pp xiii+280; £12.95 paperback.) Cambridge: Cambridge University Press, 1989. ISBN 0-521-38930-5.

Occasional Papers on Social Administration. "Hospital Closure and the Resettlement of Residents: the Case of Darenth Park Mental Handicap Hospital." L Wing. Series editor J Lewis. (Pp xv+200; £32.) Aldershot: Avebury, 1989. ISBN 0-566-07082-0.

Surviving in General Management: a Resource for Health Professionals. Ed P Fielding, P C Berman. (Pp ix+189; £8.95 paperback.) London: Macmillan, 1989. ISBN 0-333-48314-6.

History of medicine

Anaphylaxis. Charles Richet. A facsimile of the first English edition, 1913. (Pp xii+266; £21.50.) Abingdon: Oxford Historical Books, 1989. ISBN 871395-02-X.

A County Lunatic Asylum: the History of St Matthew's Hospital. D Budden. (Pp 123; figs; £4.95 paperback.) 1989. Obtainable from D Budden, Pharmacy Department, St Matthew's Hospital, Burntwood, Walsall, West Midlands WS7 9ES. ISBN 0-9515269-0-1.

Experiments and Observations on the Gastric Juice and the Physiology of Digestion. William Beaumont. A facsimile of the first edition, 1833. (Pp 280; figs; £21.50.) Abingdon: Oxford Historical Books, 1989. ISBN 1-871395-01-1.

Health, Race, and German Politics, Between National Unification and Nazism, 1870-1945. P Weindling. (Pp xi+641; figs; £55.) Cambridge: Cambridge University Press, 1989. ISBN 0-521-36381-0.

Historical Perspectives on the Role of the MRC. Essays in the History of the Medical Research Council of the United Kingdom and Its Predecessor, the Medical Research Committee, 1913-1953. Ed J Austoker, L Bryder. (Pp xi+259; £30.) Oxford: Oxford University Press, 1989. ISBN 0-19-261651-X.

History of neuroscience

History of Neuroscience. "James Parkinson: His Life and Times." A D Morris. Series editors L Marshall, F C Rose. (Pp xi+207; Sw frs 98.) Boston: Birkhäuser, 1989. ISBN 3-7643-3401-0.

The Iconographic Collections of the Wellcome Institute for the History of Medicine. W Schupbach. (Pp 71; figs and colour plates; £3 paperback.) London: Wellcome Institute, 1989. ISBN 0-85484-080-X.

The Illustrated History of Surgery. K Haeger. (Pp 288; figs; colour plates; £25.) London: Starke, 1989. ISBN 1-872457-002.

Human reproduction

Oxford Reviews of Reproductive Biology. Vol 11. Ed S R Milligan. (Pp viii+458; figs; £45.) Oxford: Oxford University Press, 1989. ISBN 0-19-857649-8.

Immunology

Chemical Immunology. Vol 46. "Antigenic Determinants and Immune Regulation." Ed E Sercarz. Series editors K Ishizaka, P J Lachmann, R Lerner, B H Waksman. (Pp xi+189; figs; £62.10.) Basel: Karger, 1989. Distributed by John Wiley and Sons. ISBN 3-8055-4960-1.

Immunology and Medicine. "Immunology of Sexually Transmitted Diseases." Ed D J M Wright. Series editor W G Reeves. (Pp xiii+274; figs; £45.) Dordrecht: Kluwer Academic, 1989. Distributed by MTP Press. ISBN 0-7462-0087-0.

Immunology and Medicine. "Mast Cells, Mediators and Disease." Ed S T Holgate. Series editor W G Reeves. (Pp xii+289; figs; £45.) Dordrecht: Kluwer Academic, 1989. Distributed by MTP Press. ISBN 0-85200-968-2.

Immunology and Medicine. "Phagocytes and Disease." Ed M S Klempner, B Styrt, J Ho. Series editor W G Reeves. (Pp x+201; figs; £40.) Dordrecht: Kluwer Academic, 1989. Distributed by MTP Press. ISBN 0-85200-842-2.

Lasers

Laser Angioplasty. Ed T A Sanborn. (Pp xi+121; figs; $49.50.) New York: Liss, 1989. Distributed by John Wiley and Sons. ISBN 0-471-50992-2.

Medical ethics

Ethics and the Health Services Manager. A Wall. (Pp ix+117; £8.95 paperback.) London: King Edward's Hospital Fund for London, 1989. ISBN 1-870551-98-2.

Medicolegal

Legal Principles and Practice in Obstetrics and Gynecology. Vol 1. Ed M Borten, E A Friedman. (Pp xi+338; figs; £38.50.) Chicago: Year Book Medical, 1989. Distributed by Wolfe Medical. ISBN 0-8151-1003-0.