

this seems a problem of minor importance. Obviously, research should continue for other antibiotics that are active against *H pylori* so that 100% eradication can be achieved.

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- 1 Graham DY. A reliable cure for Helicobacter pylori infection? *Gut* 1995;37:154-6.
- 2 De Boer WA, Tytgat GNJ. The best therapy for Helicobacter pylori infection: should efficacy or side-effect profile determine our choice? *Scand J Gastroenterol* 1995;30:401-7.
- 3 Labenz J, Ruhl GH, Bertrams J, Borsch G. Medium- and high-dose omeprazole plus amoxicillin for eradication of Helicobacter pylori in duodenal ulcer disease. *Dig Dis Sci* 1994;39:1483-7.
- 4 Logan RPH, Gummert PA, Schaufelberger HD, Greaves RRFH, Mendelson GM, Walker MM, et al. Eradication of Helicobacter pylori with clarithromycin and omeprazole. *Gut* 1994;35:323-6.

- 5 Axon ATR. The role of acid inhibition in the treatment of Helicobacter pylori infection. *Scand J Gastroenterol* 1994;29(suppl 201):16-23.
- 6 Hosking SW, Ling TKW, Chung SCS, Yung MY, Cheng AFB, Sung JY, et al. Duodenal ulcer healing by eradication of Helicobacter pylori without antacid treatment: randomised controlled trial. *Lancet* 1994;343:508-10.
- 7 Sung JY, Chung SCS, Ling TKW, Yung MY, Leung VKS, Ng EKW, et al. Antibacterial treatment of gastric ulcers associated with Helicobacter pylori. *N Engl J Med* 1995;332:139-42.
- 8 Bell GD, Powell KU, Burridge SM, Bowden AF, Atoyebe W, Bolton GH, et al. Rapid eradication of Helicobacter pylori infection. *Aliment Pharmacol Ther* 1995;9:41-6.
- 9 Bazzoli F, Zagari RM, Fossi S, Pozzato P, Alampi G, Simoni P, et al. Short-term low-dose triple therapy for the eradication of Helicobacter pylori. *Eur J Gastroenterol Hepatol* 1994;6:773-7.
- 10 Goddard A, Logan R. One-week low-dose triple therapy: new standards for Helicobacter pylori treatment. *Eur J Gastroenterol Hepatol* 1995;7:1-3.
- 11 De Boer WA, Driessen WMM, Potters VPJ, Tytgat GNJ. Randomized study comparing 1 with 2 weeks of quadruple therapy for eradicating Helicobacter pylori. *Am J Gastroenterol* 1994;89:1993-7.
- 12 De Boer W, Driessen W, Jansz A, Tytgat G. Effect of acid suppression on efficacy of treatment for Helicobacter pylori infection. *Lancet* 1995;345:817-20.
- 13 Savarino V, Mela GS, Zentilin P, Vigneri S, Celle G. Acid inhibition and amoxicillin activity against Helicobacter pylori. *Am J Gastroenterol* 1993;88:1975-6.
- 14 Hentschel E, Brandstatter G, Dragosics B, Hirschl AM, Neme H, Schutze K, et al. Effect of ranitidine and amoxicillin plus metronidazole on the eradication of Helicobacter pylori and the recurrence of duodenal ulcer. *N Engl J Med* 1993;328:308-12.
- 15 Adamek RJ, Opferkuch W, Wegener M. Modified short-term triple therapy—ranitidine, clarithromycin, and metronidazole—for cure of Helicobacter pylori infection. *Am J Gastroenterol* 1995;90:168-9.

## Thrombolytic treatment

### *Valuable in arterial thrombosis but of less certain value in venous thromboembolism*

Thrombolytic treatment has quickly established itself as effective, but doctors may have problems in drawing conclusions from the large number of clinical trials and anecdotal reports. Guidelines prepared by experts are therefore welcome—particularly on such a rapidly developing subject. The Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology has recently prepared new guidelines on the use of thrombolytic treatment,<sup>1</sup> which supersede those of the American College of Cardiology and American Heart Association.<sup>2</sup>

Unless there are clear contraindications, all patients with myocardial infarction (as diagnosed by  $\geq 1$  mm ST elevation in two or more contiguous leads or left bundle branch block in an electrocardiogram) should receive aspirin and thrombolytic treatment with a minimum of delay. Patients diagnosed as having evolving myocardial infarction should receive aspirin and have serial electrocardiography; once the above criteria are met, thrombolytic treatment should be started. The extent of the benefit clearly depends on how quickly treatment is given, particularly in the first six hours. Nevertheless, thrombolysis given as late as 12 hours after the first symptoms improves survival, and some benefit may accrue even up to 18 hours, especially in patients with stuttering infarction.<sup>3</sup>

Clear evidence exists that very early treatment maximises the benefit of thrombolysis, but neither the British task force<sup>1</sup> nor the guidelines of the American College of Emergency Physicians<sup>4</sup> recommend that thrombolytic drugs should be given outside hospital, though they might be beneficial. The British Heart Foundation's working group took a less timid view.<sup>5</sup>

These broad guidelines need slight modifications depending on the site of the infarction. The time window for thrombolysis should be wider for patients with an anterior wall infarction (which is associated with higher mortality) than for those with an infarct in other locations. Patients with inferior infarctions seem to have a poorer outcome as a result of complications of thrombolysis, but this does not apply to those in whom the infarction is associated with second or third degree heart block.<sup>6</sup>

Age over 66 was used as an exclusion criterion in many of

the clinical trials, but other studies consistently showed that the reduction in mortality was greater in those patients aged over 65 and treated with thrombolytic drugs than in control patients.<sup>7,8</sup> Thrombolytic treatment should, however, be given to older patients only after careful assessment for any potential risk of bleeding.

What about the choice of drug? One placebo controlled trial in patients treated within six hours of the onset of symptoms of myocardial infarction showed that 26 lives were saved per 1000 patients treated with 1 500 000 IU of streptokinase over 60 to 90 minutes.<sup>9</sup> An additional 9-11 lives per 1000 patients were saved in the global utilisation of streptokinase and tissue plasminogen activator for occluded coronary arteries (GUSTO) trial, which used 100 mg of alteplase in conjunction with aspirin and intravenous heparin. This treatment lowered the 30 day total mortality to 6.3%, compared with 7.2% achieved with streptokinase, aspirin, and intravenous heparin.<sup>10</sup>

In patients with peripheral arterial thromboembolism thrombolytic drugs are now usually given locally with a pulse spray technique. A rapid spray of drug through multiple holes in a catheter increases the amount of the surface of thrombus treated and simultaneously disrupts the thrombus. The result is that short occlusions (10-20 cm) are lysed within two hours, compared with 24 hours with the former slow continuous regional infusion.

Doubts continue about the use of intravenous thrombolytic drugs to treat proximal deep vein thrombosis. The trials so far published have not shown any clinical benefit either in mortality or in the incidence of the chronic post-thrombotic leg syndrome. Treatment is difficult because the mass of the venous thrombus is much greater than that in arterial occlusions and is often of mixed age. Thrombolytic drugs need to be given for a long time—sometimes days—and this increases the risk of bleeding.

Thrombolytic drugs are being recommended for acute rapidly evolving major pulmonary embolism of haemodynamic importance. Intravenous administration is said to be just as effective as the intrapulmonary route and has the advantages of simplicity and speed. There is, however, no

evidence from randomised trials that thrombolytic treatment lowers mortality in patients with life threatening pulmonary embolism.

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- 1 Ludlam CA, Bennett B, Fox KAA, Lowe GDO, Reed AW. Guidelines for the use of thrombolytic therapy. *Blood Coagul Fibrinolysis* 1995;6:273-85.
- 2 Gunnar RM, Bourdillon PDV, Dixon DW, Fuster V, Karp RB, Kennedy JW, et al. Guidelines for the early management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association task force on assessment of diagnostic and

- therapeutic cardiovascular procedures (Subcommittee to develop guidelines for the early management of patients with acute myocardial infarction). *J Am Coll Cardiol* 1990;16:249-92.
- 3 Fibrinolytic Therapy Trialists' Collaborative Group. Indications for thrombolytic therapy in suspected myocardial infarction: collaborative overview of mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;343:311-22.
- 4 Benson NH, Maningas PA, Krohmer JR, Balcombe DJ, Do RS. Guidelines for the prehospital use of thrombolytic agents. *Am J Emerg Med* 1994;23:1047-8.
- 5 De Bono DP, Hopkins A. The management of acute myocardial infarction: guidelines and audit standards. Report of a workshop of the point audit committee of the British Cardiac Society and the Royal College of Physicians. *J R Coll Physicians Lond* 1994;28:312-7.
- 6 Berger PB, Ruocco Jr NA, Ryan TJ, Frederick MM, Jacobs AK, Faxon DP, and the TIMI Investigators. Incidence and prognostic implications of heart block complication of myocardial infarction treated with thrombolytic therapy: results from TIMI-II. *J Am Coll Cardiol* 1992;20:533-40.
- 7 Grines CL, De Maria AN. Optimal utilization of thrombolytic therapy for acute myocardial infarction: concepts and controversies. *J Am Coll Cardiol* 1990;16:223-31.
- 8 Berger PB, Ryan TJ. Inferior infarction: high risk subgroups. *Circulation* 1989;81:401-11.
- 9 Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. *Lancet* 1986;ii:397-401.
- 10 GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993;329:673-82.

## Monitoring children's growth

### *New charts will help*

Children whose growth is extremely abnormal are easily recognised. The aim of growth monitoring is to identify children with less obvious but treatable growth disturbances,<sup>1,4</sup> such as growth hormone insufficiency, Turner's syndrome, and hypothyroidism.

Cheap, accurate, self calibrating equipment<sup>5</sup> such as the Leicester height measurer and better training should ensure that children are measured accurately. Interpreting measurements is more difficult: there is no easy way of separating children with true growth problems from the more numerous "short normal" children. For this, growth charts are essential.

The Tanner-Whitehouse charts, which have been used in Britain for 30 years to assess height, weight, and head circumference, are now out of date. The average height of British children has increased (the so called secular trend). The increase in breast feeding and the "humanising" of formula feeds are responsible for more rapid weight gain in the first few months of life, followed by a deceleration. Thus the typical appearance of a weight chart for an infant born in 1995 is different from that indicated by the Tanner-Whitehouse chart.

New growth charts are now available, based on seven growth surveys between 1978 and 1990.<sup>6</sup> They are called the 1990 nine centile United Kingdom charts and should replace the Tanner-Whitehouse charts. As well as describing current growth patterns more precisely, they have some new features. Firstly, they eliminate the "step" at the age of 2, when standing height is substituted for supine length. Secondly, nine centiles are now provided instead of the traditional seven. The lowest centile is the 0.4 line; only one child in 250 will fall below this line, which is a clearcut indicator for referral. Children with heights between the 0.4 line and the second centile may be normal short children of short parents but merit observation. Similarly, in a child whose height is above the 99.6 centile a growth disorder should be considered. Thirdly, the interval between each pair of centile lines is the same—two thirds of a standard deviation.<sup>7</sup> This will simplify interpretation of unusual growth patterns.

The centile lines on standard weight charts do not define a "normal" pattern of growth. Rather, they show the distributions of weights of a range of babies at various ages and are said to be cross sectional. Weight at birth and growth in extrauterine life are determined by different factors, so the weight gain of individual babies may deviate from the centile position defined by their weight at birth as they

take up their genetically determined growth trajectory.

A common problem for primary care teams is the baby whose weight gain line is crossing the centiles downwards.<sup>8</sup> Failure to thrive is suspected, but when no organic diagnosis can be made, inadequate parenting, neglect, or abuse is considered and child protection procedures may be initiated. These concerns are sometimes justified, but the diagnosis of non-organic failure to thrive is difficult<sup>9</sup> and errors can have serious consequences.

If crossing centiles can be normal, how do you decide whether a particular pattern is pathological? Conditional reference charts address this question by defining the centile ranking of the rate of weight gain over a period of time.<sup>10</sup> Substantial centile shifts turn out to be much commoner than most people imagine. Unfortunately, the extent of centile shift depends on the starting position—the more extreme the initial weight centile the greater the extent of centile shift. The charts that describe this phenomenon are inevitably more difficult to use than conventional growth charts, but the effort will be worth while and may avoid unnecessary interventions.

How do you decide if a child is too fat or too thin? Answer—use the body mass index, obtained by dividing the weight (in kg) by the height (in m) squared. The body mass index rises steeply in infancy, falls during the preschool years, and then rises into adulthood. It must therefore be related to age and yet another set of new charts enables this to be done.<sup>11</sup> The role of these charts in clinical practice has yet to be determined. An extreme centile position does not necessarily indicate disease. The age at which the slope of the body mass index curve changes from down to up (the age of "adiposity rebound") predicts adult fatness—the earlier the rebound the greater the risk of adult obesity. Whether this pattern could be changed by better diet or more exercise in early childhood is a question for long term research.

The 1990 nine centile charts, the conditional reference curves, and the charts of body mass index come from the same dataset of measurements on white children only. The number of non-white children measured in the various samples was small; furthermore, the influence of social class and the extent and rate of the secular trend vary among ethnic groups. Construction of growth charts for them all would be almost impossible. Data are available, however, on racial differences in growth and body build.<sup>6</sup>

Monitoring growth is easy to do but difficult to do well.<sup>12</sup> An investment in the training of primary care staff should