

POP GOES THE WEASEL

Bandolier was reading a review while trawling for interesting articles for these pages and was struck by the sheer number of weasel words that keep appearing. These are words like "may" and "should", and phrases such as "could be expected to", "it would appear that", and so on.

Perhaps it was a bad day, but distinctly lacking were solid word like "will" or "can", and definitive phrases like "will cure" or "will harm".

Much of our medical literature is plagued by weasel words, which we all use from time to time because there is always some circumstance in which a definite statement can be proved to be incorrect. Such is the complexity and diversity of medicine, and our natural caution about being wrong.

The trouble is that overcautiousness will lead to confusion. *Bandolier* saw one sentence which read something like "such-and-such drug may result in fewer side effects". Did this mean that the author *knew* that the drug would give fewer side effects, but was being cautious, or did the author *have no idea* that such was the case, but thought it possible? Readers could interpret it in any way they chose - not, perhaps, the result that was intended.

It is just this sort of confusion that systematic reviews based on randomised controlled trials help dispel. Weasel words can be replaced with numerical estimates with confidence intervals. Cure or harm become quantifiable and understandable, rather than matters of opinion.

So *Bandolier* is going to try to stop using weasel words in its columns. This won't be easy, and we will be grateful for readers spotting those that get away.

SYSTEMATIC REVIEW OF INTRAVENOUS REGIONAL SYMPATHECTOMY FOR REFLEX SYMPATHETIC DYSTROPHY

Chronic non-malignant pain is often difficult to treat, and performing randomised controlled trials (RCTs) in persons with these pains raises many practical and ethical problems. A major difficulty is the high placebo response rates often found by RCTs - which is why placebo-controlled trials are necessary in these conditions.

Over 120 years ago a syndrome of persistent burning pain and trophic changes called causalgia was noted in the limbs of soldiers after gunshot wounds. The term reflex sympathetic dystrophy (RSD) is now used to describe a number of chronic pain conditions associated with altered activity of the sympathetic nervous system. RSD may be the extreme end of a spectrum of conditions associated with damage to nerves after trauma.

The clinical reality is a "funny pain" in a "funny looking" limb. The diagnosis suggests that a disordered nervous system causes the pain - but it may be that the pain causes a disordered nervous system.

How common is RSD?

The incidence of RSD among patients in a tertiary referral centre is about 2 - 5%. In the general population the incidence is of the order of 10 per million population.

How is RSD treated?

A common treatment is intravenous regional sympathetic blockade (IRSB). This involved injecting a high concentration of a drug known to block the sympathetic nervous system (guanethidine in the original report) into a limb isolated with a tourniquet.

Does IRSB work?

There have been few RCTs. Those that have been done have been collected into a systematic review together with a new RCT [1]. There were seven controlled trials with guanethidine, reserpine, bretylium, droperidol or ketanserin. Sample sizes ranged from six to 21 patients.

Five of the seven RCTs in the systematic review failed to show a significant analgesic difference between the IRSB and control groups. The new RCT in the paper was stopped early because of a significant incidence of severe adverse effects. The analysis did not show any analgesic effect of IRSB.

Should IRSB be bought by purchasers?

Almost certainly not. This is a complicated subject with many nuances, but the collected evidence indicates that the procedure is without significant analgesic effect but with potentially dangerous adverse effects.

That does not mean that there is not a research agenda. Patients with RSD have few effective treatment options, and

it may be that there are elements in the procedure - perhaps the tourniquet itself in some patients - which could provide relief. We need to know what they are.

Reference:

- 1 AR Jadad, D Carroll, CJ Glynn, HJ McQuay. Intravenous regional sympathetic blockade for pain relief in reflex sympathetic dystrophy: a systematic review and a randomised, double-blind crossover study. *Journal of Pain and Symptom Management* 1995 10: 13-20.

FOOD FOR THOUGHT: CHOLESTEROL LOWERING IN PATIENTS WITH CORONARY HEART DISEASE

Does lowering serum cholesterol improve survival in patients with coronary heart disease (CHD)? This loaded question may now be answered following the results of an in-depth study from Scandinavia, the 4S study [1].

Setting

Men and women aged 35-70 years with a history of angina or acute myocardial infarction (MI) were screened for eligibility. If none of the exclusion criteria applied and the patient consented, fasting serum cholesterol and triglyceride were measured. If, after 8 weeks of dietary advice cholesterol was 5.5 - 8.0 mmol/L or triglyceride over 2.5 mmol/L, patients were randomised to simvastatin 20 mg or placebo to be taken before the evening meal.

4444 patients were so randomised between May 1988 and August 1989, and were followed up for a median of 5.4 years with frequent clinic visits for lipid and other measurements.

Outcomes

The primary endpoint was mortality. The secondary endpoint was a major coronary event - coronary death, non-fatal MI, resuscitated cardiac arrest and silent MI confirmed by electrocardiogram.

The tertiary endpoints were any coronary event (secondary endpoint plus cardiac revascularisation procedures), non-coronary atherosclerotic events, incidence of heart operations and hospital admission for acute CHD without a diagnosis of MI.

Results

Lipid concentrations showed little change in the placebo group over three years except for triglycerides,

which rose by 7%. In the simvastatin group over the whole course of the study there were substantial (25-35%) falls in total and LDL cholesterol, a small (10%) fall in triglycerides, and a small but useful increase of 8% in HDL cholesterol. Doses needed to be increased to 40 mg a day in 37% of patients.

There were fewer deaths, and especially coronary deaths, in the treated patients (see box). The NNT for simvastatin to prevent a coronary death was 29.

There were fewer non-fatal coronary events in the treated patients. The NNT to prevent a major coronary event was 15. Fewer treated patients had coronary surgery or angioplasty. The NNT to prevent one episode of coronary surgery was 17. Overall secondary endpoints were much reduced in treated patients. The NNT to prevent any secondary endpoint was 12.

The overall frequency of adverse effects was similar in the two groups, with 6% in each group discontinuing treatment because of adverse effects. A single case of rhabdomyolysis occurred in one woman taking simvastatin. It resolved when treatment stopped.

Conclusion

This is an important study, well conducted over many years, collecting a very considerable amount of information on many patients. The question now is whether cholesterol lowering should be a target in all patients with coronary heart disease and serum cholesterol >5.5 mmol/L?

Addition of simvastatin to the treatment regimens of 100 CHD patients would yield the following benefits over the first six years: preservation of the lives of four of the nine patients who would otherwise die of CHD; prevention of non-fatal MI in seven of an expected 21 patients; avoidance of revascularisation procedures in six of the 19 patients in which it would otherwise be done.

The 4S study will take a little while to digest, but will aid considerably those working on guidelines.

Results of the 4S Study

Outcome	Placebo N=2223	Simvastatin N=2221	NNT (95% CI)
All death	256	182	30 (18 - 70)
Coronary death	189	111	29 (18 - 56)
Major coronary event	502	353	15 (10 - 25)
Any secondary endpoint	622	431	12 (9 - 18)
Coronary surgery/ angioplasty	383	252	17 (12 - 28)

Economic analysis

The economic analysis remains to be published. The report contains all the details needed for a quick “back of envelope” estimate of whether there are any economic benefits from introducing this expensive treatment. What NNT is needed for economic benefits to accrue?

Reference:

- 1 Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994 344: 1383-9.

AUDIT FACILITATORS IN CHILDHOOD ASTHMA

Bandolier actively looks for examples of effectiveness in management. An excellent example of a controlled trial of an audit facilitator in the diagnosis and treatment of childhood asthma in general practice is well worth a read [1]. It was set up to test the hypothesis that an audit facilitator could change the pattern of diagnosis and treatment of childhood asthma.

Setting and design

The setting was 12 general practices in Tayside, with 73,000 patients, 12,500 of whom were aged 1 - 15 years. Children in the practices were stratified by age and then randomised into intervention and control groups within each practice. Children chosen were those with histories suggestive of asthma - about 1,500 each in the intervention and control groups.

The intervention comprised provision of information and equipment required for each practice to offer all the children in the intervention group a systematic or opportunistic review, follow up, assessment, educational material and emergency treatment.

Those in the intervention group had a project sticker on the front of their case records. Attached to the records were a chart for asthma diagnosis, a protocol for managing asthma attacks, a letter suggesting that the GP review the patient and guidelines on treatment.

Outcomes

For review, year 1 was the 12 months before the facilitator’s visit to the practice, and year 2 the 12 months following the visit. Recorded were:

- practice initiated consultations
- patient initiated consultations
- structured asthma assessments

- diagnosis of asthma
- prescriptions of respiratory drugs
- type and cost of prescriptions
- admissions and attendances at outpatients and A&E.

Results

This paper contains excellent analysis and results. Compared with controls the intervention group had more practice initiated consultations for asthma, more new diagnoses of asthma, and were more frequently prescribed inhaled cromoglycate.

In the intervention group hospital inpatient days fell from 155 to 122, but rose from 69 to 117 in the control group between the year before and the year after study.

Total primary care and secondary care costs rose by 4.4% in the intervention group, but rose by 13.9% in the control group (see box). This was without the salary costs of the facilitator, and conclusions about the long-term overall economic impact of this type of intervention need more analysis than the paper was able to give - mainly because these were snapshot estimates which could well change with longer term improved awareness.

Costs of asthma care (£)

	Intervention Group (N = 1585)		Control Group (N = 1563)	
	Year 1	Year 2	Year 1	Year 2
Primary care	30,118	37,243	29,131	27,990
Hospital care	25,406	20,727	12,699	19,650
Total	£55,524	£57,970	£41,830	£47,640

Reference:

- 1 FP Bryce, RG Neville, IK Crombie, RA Clark, P McKenzie. Controlled trial of an audit facilitator in diagnosis and treatment of childhood asthma in general practice. *British Medical Journal* 1995 310: 838-42.

IV STEROIDS IN ACUTE SEVERE ASTHMA

The current British Thoracic Society guidelines [1] on the management of acute asthma recommend the use of oral prednisolone or “intravenous hydrocortisone if severely ill or vomiting”. It is common practice to administer 100-200 mg of intravenous hydrocortisone in accident and emergency departments to any asthmatic likely to need admission.

Several studies suggest that intravenous steroids confer no additional benefits over oral steroids in this situation. The main findings of four trials are reported here.

Stein & Cole [2] randomised 81 patients with acute asthma to receive either 125 mg methylprednisolone or normal saline intravenously within 30 minutes of presentation. All patients received oral prednisolone 40 mg at 6 hours and standard bronchodilator therapy. No difference was found in duration of emergency room treatment, hospitalisation or return visits.

Morell et al [3] randomised 90 patients with acute severe asthma to receive intravenous methylprednisolone 10 mg/kg four-hourly for 48 hours, or 2 mg/kg four-hourly for 48 hours, or placebo. All patients received standard bronchodilator therapy. No difference was found at 48 hours in FEV1, FVC, PEF or arterial oxygen or carbon dioxide tension.

Rodrigo & Rodrigo [4] randomised 98 patients with acute asthma to receive either intravenous hydrocortisone 500 mg or placebo in addition to bronchodilator therapy. They recorded no difference in duration of emergency room treatment or hospitalisation at six hours.

Harrison et al [5] randomised 52 patients to receive intravenous hydrocortisone 3 mg/kg bolus, 3 mg/kg six-hourly or placebo. All patients received prednisolone 45 mg orally followed by 15 mg eight-hourly plus bronchodilator therapy. There was no difference in peak flow measurements at 24 hours.

Conclusion

While there is no doubt about the effectiveness of steroids in the management of chronic asthma, there is at least a question over their usefulness in the management of acute asthma. Prednisolone is readily absorbed from the stomach and achieves peak plasma concentrations in about 15 minutes. The routine use of intravenous steroids in patients with acute asthma who can take oral steroids should be discontinued.

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References:

- 1 British Thoracic Society. Guidelines for the management of asthma in adults: II - Acute severe asthma. *Thorax* 1992 47: suppl.
- 2 LM Stein, RP Cole. Early administration of corticosteroid in the emergency room treatment of acute asthma. *Annals of Internal Medicine* 1990 112: 822-7.
- 3 F Morell, R Orriols, J de Garcia, V Currull, A Pujol. Controlled trial of intravenous corticosteroids in severe acute asthma. *Thorax* 1992 47: 588-91.
- 4 C Rodrigo, G Rodrigo. Early administration of hydrocortisone in the emergency room treatment of acute asthma: a controlled clinical trial. *Respiratory Medicine* 1994 88: 755-61.
- 5 BDW Harrison, GJ Hart, NJ Ali, TC Stokes, DA Vaughan, AA Robinson. Need for intravenous hydrocortisone in addition to oral prednisolone in patients admitted to hospital with severe asthma without ventilatory failure. *Lancet* 1986 i: 181-4.

TRANSURETHRAL PROSTATECTOMY FOR BENIGN PROSTATIC HYPERPLASIA

In January *Bandolier* featured the AHCPR report [1] on benign prostatic hyperplasia (BPH). BPH is becoming a hot topic, and some recent papers help to shed new light on treatment choices - and especially watchful waiting.

Treatment in transition

BPH is a condition where there is beginning to be a wide range of treatment options, compared with the previous situation where transurethral resection of the prostate (TURP) was the main treatment option. These treatment options, not all of which are yet backed by randomised controlled trial evidence, are well laid out and reviewed by Joseph Oesterling [2], a widely respected US urologist.

There are new medical therapies. 5-alpha reductase inhibitors reduce the conversion of testosterone to dihydrotestosterone, and alpha-adrenergic antagonists block the adrenergic receptors in hyperplastic prostatic tissue so that smooth muscle tone of prostatic structures is decreased.

There are new minimally invasive surgical techniques - prostatic stents, transurethral incision of the prostate, microwave therapy and laser prostatectomy.

Which is best? A good question with, unfortunately as yet no clear answers. Oesterling's review at least brings the reader up to date with the most recent techniques and their results - though not on an evidence-based basis.

RCT of TURP and watchful waiting

There are few randomised controlled trials of TURP. A recent multicentre study [3] compared watchful waiting with TURP in men aged over 54 years (average 66 years) with moderate symptoms of BPH. Using a symptom scoring system with a maximum score of 27 points, those with scores of 10 - 20 points were eligible (see *Bandolier* 11).

Men were randomised to watchful waiting (276) or TURP (280), which was carried out within two weeks of randomisation. They were seen at six to eight weeks, and then twice a year for three years of follow-up.

The primary outcome measure was treatment failure, defined as any of the following events:-

- death
- repeated or intractable urinary retention
- residual urinary volume of over 350 mL
- development of bladder calculus
- new, persistent incontinence
- a symptom score of 24 or higher at one visit
- a symptom score of 21 or higher at two consecutive visits
- doubling of baseline serum creatinine

Immediate postoperative results of TURP

There were no deaths associated with surgery. In the first 30 days after surgery there were no complications in 91% of men treated. The most frequent complications were placement of another urinary catheter (3.7%), perforation of the prostate capsule (2%) and haemorrhage requiring transfusion (1%). Prostate cancer was found in 10% of the specimens removed at surgery.

Treatment outcomes after 3 years

The treatment outcomes are shown in the box. Treatment failure was more common in watchful waiting, as was high residual urinary volume and the occurrence of a high symptom score. The failure rate in the watchful waiting group was 6.1 per 100 person years compared with 3.0 per 100 person years in the surgery group. The difference was largely due to intractable urinary retention, high residual volume and high symptom score.

Men who underwent TURP had a larger 3-year fall in symptom score (mean 10 points) than did those with watchful waiting (mean 5.5 points). They also had an increase in peak urinary flow rate of 6 mL/sec (to 18 mL/sec), compared with watchful waiting where the urinary flow rate at three years was 13 mL/sec, unchanged from baseline.

There were also some benefits in quality of life scores for men who underwent TURP - mainly in terms of less bother from urinary difficulties and improvements in daily living.

Treatment outcomes after three years of follow-up

Outcome	Surgery (N=280)	Watchful waiting (N=276)	Relative risk (95% CI)
Treatment failure	23	47	0.5 (0.3 - 0.8)
Death	13	10	1.3 (0.6 - 2.9)
Urinary retention	1	8	0.1 (<0.1 - 0.9)
High residual volume	3	16	0.2 (0.1 - 0.6)
Persistent incontinence	4	4	1.0 (0.3 - 3.9)
High symptom score	1	12	0.1 (<0.1 - 0.6)

Who benefits?

A key message was that men who were most bothered by their symptoms at baseline benefited most from surgery. 91% of those who were substantially bothered by urinary difficulties at baseline had improvements, as compared with 62% of those who were less bothered. In the men assigned to watchful waiting, 48 of 155 men (31%) who were most bothered by their symptoms went on to surgery compared with 16 of 97 (16%) of men who were less bothered by their symptoms.

Take-home message from the RCT

Men with moderate symptoms of benign prostatic hyperplasia that substantially reduce the quality of their lives have most to gain from transurethral resection. For men who are less bothered by urinary difficulties, watchful waiting is a safe alternative.

TURP in the UK - deaths and complications

It is always useful to know the risks and benefits of any treatment, especially an operation. Some of the benefits of TURP compared with watchful waiting have been explored by the US RCT. However, this was a multicentre study in the US Veterans Medical Service, one of the best. There were no deaths associated with surgery, though other surveys have found death rates of about 1%.

A recent survey of deaths and complications following prostatectomy in 1400 men in the Northern Region paints a more realistic picture of prostatectomy in Britain [4]. This study looked at 12 hospitals which undertook prostatectomy for an eight month period in 1991. An independent audit was carried out according to a predetermined protocol by two clinical co-ordinators who examined case notes three months after the operation.

The outcomes collected were early mortality (fewer than 30 days after operation) and late mortality (30 - 90 days after operation). Morbidity measures were return to theatre (for haemorrhage, clot evacuation and early reoperation for failure to void), a blood transfusion of two or more units

and the development of postoperative sepsis.

Results from 12 hospitals

A total of 1431 operations were performed, 97.6% transurethrally, the remainder being retropubic prostatectomies. One hospital per-

formed over 450 operations, four others over 100 operations and seven hospitals fewer than 100 operations.

Mortality

The early mean death rate was 13 of 1396 patients (0.9%). There was a wide intersite variation, from 0 to 3.8%. There was a small bias in favour of hospitals performing over 100 operations (0.5%) compared with those performing fewer than 100 operations (1.7%). Early mortality was lower in elective admissions (0.5%) than in emergency admissions (2.4%).

Morbidity

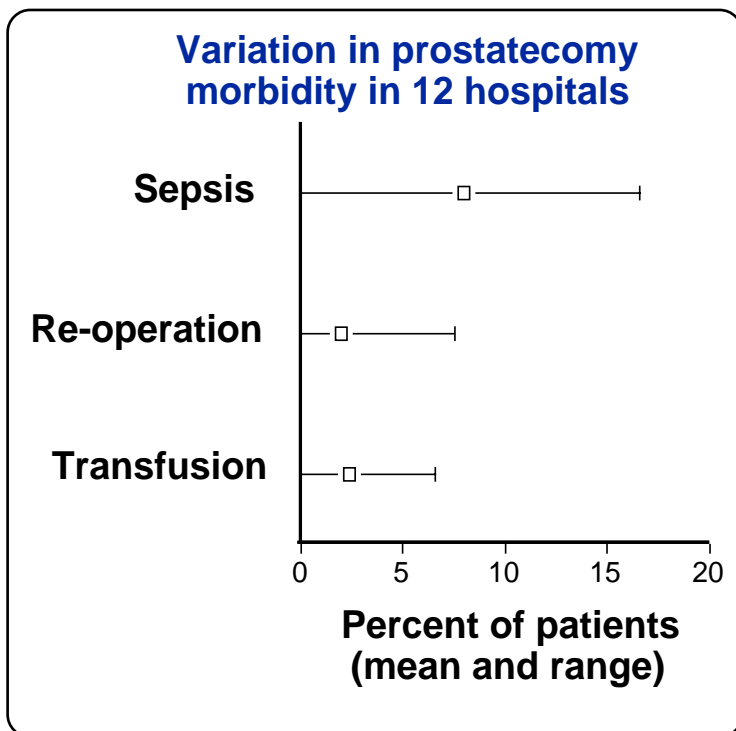
Overall 2.4% of patients needed a blood transfusion. There was a six-fold variation in transfusion rate across the 12 sites (0 - 6.6%).

A mean of 2% of patients were returned to theatre soon after operation for bleeding, clot evacuation and early repeat TURP. There was a seven-fold variation in early re-operation across the 12 sites (0 - 7.5%).

The mean incidence of postoperative sepsis was 8%. There was a 17-fold variation in sepsis rate across the 12 sites (0 - 16.9%).

Significantly more complications were found in low volume compared with high volume sites. Hospitals where fewer than 100 patients were treated had an average of 0.46 complications / patient compared with 0.24 complications per patients in hospitals performing more than 100 operations.

Take-home message



The authors conclude with a simple take-home message. Variation exists, there are reasons for it, audit demonstrates it, action changes it, and purchasers and providers should be aware of it.

References:

- 1 JD McConnell, MJ Barry, RC Bruskevitz et al. Benign prostatic hyperplasia: diagnosis and treatment. AHCPR Department of Health and Human Services, Rockville Md USA.
- 2 JE Oesterling. Benign prostatic hyperplasia. Medical and minimally invasive treatment options. New England Journal of Medicine 1995 332: 99-109.
- 3 JH Watson, DJ Reda, RC Bruskevitz et al. A comparison of transurethral surgery with watchful waiting for

moderate symptoms of benign prostatic hyperplasia. New England Journal of Medicine 1995 332: 75-9.

- 4 AC Thorpe, R Cleary, J Coles, S Vernon, J Reynolds, DE Neal. Deaths and complications following prostatectomy in 1400 men in the Northern Region of England. British Journal of Urology 1994 74: 559-65.

ANTIMICROBIAL TREATMENT OF CYSTITIS

Bandolier #13 carried a report [1] from a recent issue of JAMA concerning a randomised controlled trial of various antimicrobial drugs in the treatment of cystitis in young women. The study, which included an interesting economic analysis, concluded that trimethoprim-sulfamethoxazole produced the highest cure rate of drugs tested and was cheapest. Trimethoprim alone was not tested.

A number of readers have pointed out that there is no convincing evidence that this combination is any more effective than trimethoprim alone, and that the combination may carry a higher rate of adverse effects, especially in the elderly. They also point out that present prescribing policies in the UK favour trimethoprim alone rather than the combination, and that prescribing advice to GPs is to restrict their use of Co-trimoxazole on the grounds of safety.

Trimethoprim vs. Co-trimoxazole

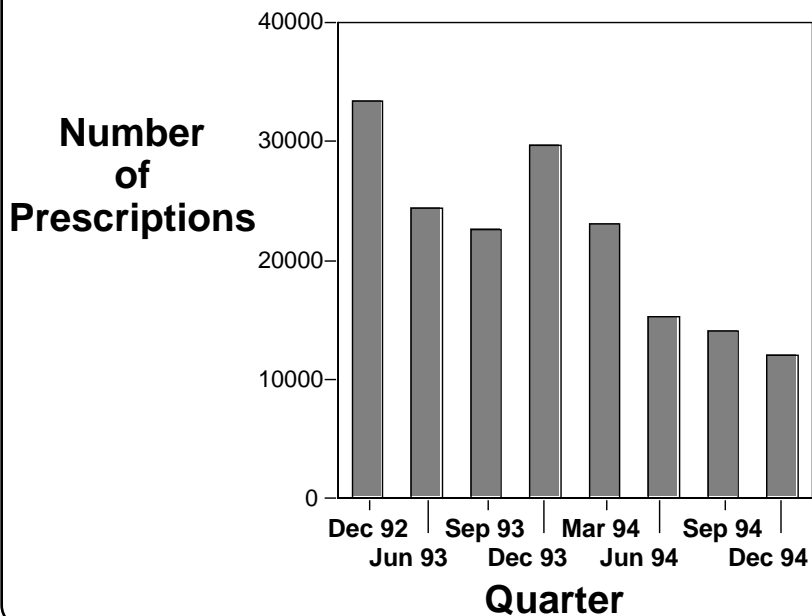
A randomised controlled double blind trial of trimethoprim alone versus Co-trimoxazole [2] showed no difference in efficacy between the two treatments in the urinary tract infection. Overall results in general practice patients, hospital patients and pregnant women gave an overall cure rate for trimethoprim of 89% (59 of 66 patients) and 84% (58 of 69 patients) with Co-trimoxazole.

Adverse effects were worse for Co-trimoxazole, where 17 of 83 patients treated (21%) had unwanted effects. With trimethoprim only 7 of 84 patients treated (8%) had unwanted effects.

More adverse effects with Co-trimoxazole

DTB in 1986 [3] indicated that deaths from Co-trimoxazole and trimethoprim were rare - about 1 per million prescriptions. About 80% were due to blood dyscrasias and 20% to skin reactions. With Co-trimoxazole deaths per million were 15 times higher in patients aged 65 or over than in those under 40 years. With trimethoprim, DTB indicated that there were no reports of toxic epidermal necrolysis.

Co-trimoxazole prescriptions by GPs in Wales



CORRESPONDENCE

Sirs,

In UK general practice the choice of antibiotic is often made, and treatment commenced, before the laboratory report on the susceptibility of the causative organism is available. Knowing the probable infecting organism and its likely susceptibility is required. It is essential to base prescribing policy on local statistics in view of geographical variations which are known to occur [1].

A recent review of antibiotic policies and their relevance to general practice prescribing [2] suggests that in the UK rational antimicrobial prescribing requires effective communication between the FHSA, microbiologists and GPs. Antimicrobial prescribing guidelines in the treatment of urinary tract infection were produced in Leices-

tershire and Derbyshire. The Leicestershire guidelines, based on local susceptibility data, drew attention to the substitution of trimethoprim alone for Co-trimoxazole.

In Epsom and Ewell in Surrey, 83% of urinary isolates from GPs (total 4082) in 1994 were coliforms. A breakdown of antibiotic sensitivities to coliforms showed 58% sensitivity to amoxycillin, 76% to trimethoprim, 90% to nitrofurantoin, 95% to cephalexin and 100% to ciprofloxacin (S Chambers, PHL Epsom, personal communication).

A cost analysis reveals that if the first-line treatment of patients with a coliform UTI (3394 isolates) was trimethoprim 200 mg twice a day for five days (cost of course £0.38), this would cost the locality £1,289. If the remaining 24% of patients who were resistant were then treated with cephalexin 500 mg three times daily for five days (cost of course £3.60) the combined cost would be £4,220. The cost of using cephalexin as first-line on all patients would be £12,218.

Both treatments would leave about 5% of patients resistant to treatment, though using trimethoprim first-line would result in saving £7,998 for the treatment of urinary tract infections in Epsom and Ewell. Given the development of locality purchasing, such cost analyses are becoming increasingly important.

In broad terms this suggests that to ensure an extra 20% of women receive an antibiotic to which they are sensitive would cost three times as much, against the price of a few extra days of discomfort.

We realise, of course, that sensitivities are in-vitro findings and may not always correlate with clinical response. However, the main message must be that rational prescribing of antimicrobials (that which is effective, appropriate, safe and economical) requires knowledge of local data, effective communication between GPs and microbiologists, and knowledge of the safety profiles of the drugs used.

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First choice

The MeReC Bulletin [4] looked at simple urinary tract infections in 1990. It concluded that trimethoprim is an appropriate first choice treatment, a view confirmed by more recent reviews [5].

Pharmaceutical advisers to FHSA's throughout the UK have been attempting to persuade GPs to restrict their use of Co-trimoxazole. *Bandolier* is indebted to Dr Bryn Davies of the South Glamorgan Health Authority for pointing out that this is one topic where pharmaceutical advisers have been successful, with prescriptions by GPs in Wales dropping significantly in 1994.

Bandolier thanks all those who wrote about this topic and pointed out what one correspondent called "a fall from grace"!

References:

- 1 TM Hooton, C Winter, F Tiu, WE Stamm. Randomized comparative trial and cost analysis of 3-day antimicrobial regimens for treatment of acute cystitis in women. *Journal of the American Medical Association* 1995 273: 41-5.
- 2 W Brumfitt, R Pursell. Double-blind trial to compare ampicillin, cephalexin, co-trimoxazole, and trimethoprim in treatment of urinary infection. *British Medical Journal* 1972 2: 673-6.
- 3 Co-trimoxazole, or just trimethoprim? *Drug and Therapeutics Bulletin* 1986 24: 17-19.
- 4 Simple urinary tract infections. *MeReC Bulletin* 1990 1: 21-3.
- 5 M Gill. Use of sulphonamides and trimethoprim today. *Prescriber* 1995 Feb 5: 55-62.

TREATMENT OF HYPERTENSION IN THE ELDERLY

A number of drug treatments were used, including thiazides, reserpine, atenolol, β -blockers and methyldopa.

Bandolier is keen on numbers-needed-to-treat (NNTs) as a simple way of describing complicated information. There are, however, times when examining the complicated detail is as important as looking at the simple take home message. Such is the case with a paper on hypertension in the elderly [1].

Take home message

For readers whose minds feel stretched enough already, the message of this excellent systematic review and meta-analysis is that treatment of hypertension in elderly people is a treatment with "strong, consistent and convincing" evidence of effectiveness. Only eighteen subjects have to be treated to prevent one vascular (cerebrovascular or cardiovascular) event (NNT = 18).

Systematic review

This review [1] involved 13 trials of 16,500 elderly patients aged 60 years or older, lasting at least one year and which evaluated effects of drug treatment on morbidity or mortality outcomes.

Coronary heart disease mortality included fatal myocardial infarctions and sudden or rapid cardiac death; morbidity included non fatal infarctions. Cerebrovascular mortality and morbidity included fatal and non fatal strokes respectively. Cardiovascular mortality summed coronary heart disease and cerebrovascular disease, but also included aneurysms, congestive heart failure and transient ischaemic attacks.

Results

Results are presented in diagrams which include odds ratios and NNTs, an at-a-glance review of the evidence. There is also an interesting split in the analysis, comparing recent, large, high-quality trials with all trials to show the effect of quality. The high quality trials tended to produce more positive results. A summary of the results is shown in the box.

The overall NNT to prevent one cardiovascular event was 18 (95% CI 14 - 25) patients to be treated for five years. To prevent coronary heart disease the NNT was 61 (39 - 141) and to prevent cerebrovascular disease the NNT was 43 (31 - 69).

Stretching the mind

The real mind-stretcher here is that the authors go on to extend their observations to younger and middle-aged subjects, where the results are not so positive. However, the comparison and discussion raises the possibility that long-term cumulative benefits in younger persons with greater remaining life expectancy and fewer competing risks may exceed those in older persons.

For those treating patients with hypertension, this paper is very much worth reading.

Reference:

- 1 CD Mulrow, JA Cornell, CR Herrera, A Kadri, L Farnett, C Aguilar. Hypertension in the elderly. Implications and generalizability of randomized trials. *Journal of the American Medical Association* 1994 272: 1932-8.

NNTs for treating hypertension in the over-60s

	Number-needed-to-treat High Quality Trials	All Trials
Cardiovascular mortality	52	58
Cardiovascular morbidity & mortality	18	21
Cerebrovascular mortality	183	193
Cerebrovascular morbidity & mortality	43	46
Coronary heart disease mortality	78	88
Coronary heart disease morbidity & mortality	61	68