but many new features will be added in 1999 on a new life. The familiar Internet changing, and the Internet version of academic journals – dominate medical publishing, rather than the impact that can be made by doing simple things right.

We are delighted, therefore, to announce Bandolier’s sister publication ImpAct, which is bound into this month’s issue, and will be for the rest of 1999. ImpAct – for impact and action – will be published every two months. If Bandolier is at the harder end of the spectrum looking at clinical evidence, ImpAct will be at the softer but perhaps more difficult implementation end. It aims to seek out the unsung heroes and heroes of the NHS who have developed methods of delivering high quality service, and to spread the word of how they have done it.

Red Baron to BA

It has been said that the “NHS is set up to fail”. Despite our best efforts the system frustrates our attempts to improve quality because it is complex, ponderous and divided by artificial boundaries. There are many “aces” managing to excel despite this. The need is to change the systems so that everyone can succeed. We need to find ways to share our experiences of success in good practice, and to support learning across the NHS. ImpAct will be one small part of this.

Electronic Bandolier

April saw the first steps along a new path for the electronic version of Bandolier. Until now it has largely been the collected issues of Bandolier in electronic format. This is now changing, and the Internet version of Bandolier will take on a new life. The familiar Internet Bandolier is still there, but many new features will be added in 1999.

♦ We have opened Bandolier’s Knowledge Bazaar. This involves grouping the many subjects we have covered over the last six years under different headings – healthy living, alternate medicines, heart, gastrointestinal, HIV/AIDS, diagnostics and so on.

♦ We are exploring ways to give every electronic reader access to PDF files of every Bandolier edition. PDF stands for portable document format. It means that if you have the free software Acrobat reader version 3.0 or above on your computer you can download a file across the net. When opened on your computer you have a facsimile of the paper version of Bandolier which you can print yourself. Instructions on how to do this will be given, and you will be able to create a searchable folder on your own system.

♦ We are hosting ImpAct from May 1999 onwards. In the immediate future this will be just the journal plus links. We will try to increase this to become a more comprehensive learning source.

♦ We are seeking external sources of good quality information for the site. In April we put up PDF files of the excellent “What is” series from Rhone Poulenc Rorer and Hayward Medical, and they are available now.

♦ Most important, we are looking to collect together and précis systematic reviews in particular subject areas. On July 14 1999 we will open the Oxford Pain Site. This will have summaries of about 100 systematic reviews in pain – all with a clinical bottom line at the top to be read in about 15 seconds, and with a two to 10 minute read to follow if you want. There will also be essays on methods, about using the information, and about harmful effects. The “jewel in the crown” will be the Oxford League Table of acute pain – NNTs from systematic reviews of just about every analgesic intervention for which there is available data.

The Bandolier Internet site has been run for five years without any resource backing from the NHS. We have been able to make this extra progress with no-strings financial support from the BUPA Foundation and from Merck, Sharpe and Dohme. We will seek further funding to maintain and expand the site by adding information that fails to get into the paper version for lack of space.

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The views expressed in Bandolier are those of the authors, and are not necessarily those of the NHSE.

Bandolier Internet publications www.jr2.ox.ac.uk/Bandolier
Getting Bandolier and ImpAct

Though we have many readers, we still find people who would like Bandolier but don’t get it. Bandolier and ImpAct are free in the NHS, except Scotland and Northern Ireland. The copies are bought for you, at the cost of production, by Regional R&D Directorates. While many people write appreciative notes to Bandolier, it would be nice to thank them for their support, so drop them a line.

With the new NHS structures in place, this might be a time to reconsider how (or if) Bandolier is distributed in your PCG or Trust. Does every GP get a copy, or practice nurse, or pharmacist? Should ImpAct and Bandolier be distributed more widely in your Trust? Does your hospital Intranet mirror the Bandolier Internet site?

All of this is easy to arrange. You can fax or email the Bandolier office (contacts on the back page), and we will make the necessary arrangements. The cost of producing these journals is probably less than the cost of photocopying them. Bandolier is already mirrored on Intranets in Wales, Oxford, and elsewhere. Email us if you want it in your hospital.

Back numbers

If you would like to use back numbers of Bandolier for teaching or other purposes, please send a cheque for £10 made out to Oxfordshire Health, and we will send you those copies we have available over the past year.

Evidence-Based Practice and Clinical Governance

This workshop is aimed at health care professionals who want to develop or expand their understanding and skills in evidence-based practice. The workshop will be especially useful for those involved in developing clinical governance, in quality improvement or in clinical teaching. The fee for the workshop is £600, inclusive of five nights (5-10 September) bed, breakfast, and lunch, conference dinner, and welcoming barbecue on Sunday. All fees are payable in advance.

Further information and enquiries:
Dr Toby Lipman, Westerhope Medical Group, 377 Stamfordham Road, Newcastle upon Tyne. NE5 2LH.
Tel. 0191 243 7000. Email: toby@tobylipm.demon.co.uk

Acting on the Evidence

This is a one-day symposium being held at the Staffordshire General Hospital on Tuesday 28th September. It has an impressive list of speakers, including both those at the coalface – “EBM at 2.00 am”, and those responsible for policy. It looks like a stimulating day for £175. For details contact Janet Watson – Tel 01785 230640; Fax 01785 230620.

Corneal abrasion treatment

If someone suffers a corneal abrasion through an accident, does padding the eye with an eye patch help it heal? The answer from a systematic review [1] is that eye patches are a waste of time.

Review

A very thorough searching process (including contacting authors for data) sought randomised trials (mainly in English) which had the following criteria:

- Compared an eye patch with no eye patch for at least 24 hours.
- Primary outcome was time to resolution of the abrasion and pain.
- Patients at least 6 years of age.
- Abrasion due to traumatic injury or removal of a foreign body (but not contact lenses).

Results

Seven trials (with 608 patients) were found, three of which used fluorescein to assess healing and four used a slit lamp. Eye patches were of several types, but in essence all used cotton wool, gauze, pads or bandages taped over the eye to keep it closed. Most studies were in emergency departments or eye hospitals. Follow up was generally thorough. Outcomes were generally assessed by observers aware of treatment.

Five trials had data for analysis. Healing rates at days 1 and 2 are shown in the Figure (page 3). There was no statistical difference either at day 1 (relative risk 0.87; 0.68 to 1.13) or at day 2 (1.01; 0.65 to 1.55). For pain, two of the six studies which measured it found less pain in the unpatched group. Complications were few (four in the padded group, two in the non padded patients).

Comment

A simple question, this, and it is interesting to see that at least eight trials have looked at it (a pity that one Danish paper was not included). Given how fiddly eye patches are, the knowledge that they are no use and can be dispensed with is worthwhile. Bandolier’s Scandinavian correspondent supplied the Danish reference [2] which was not included, and which compared chloramphenicol ointment plus patch for six hours followed by chloramphenicol drops for six days with chloramphenicol ointment plus double eye patches for 24 hours. The conclusion was that double eye patches were better, but the groups were small, and exclusions were high. This trial would not have altered the overall conclusions.

Reference:
An immediate response to problems of diagnostic testing strategies is that of entrenched routine. “We always do this” is a powerful argument, especially when no-one can remember why it is done. Who wants to rock the boat, after all? So examples of how to make some sense of a testing strategy should be cherished. A nice example comes from Groote Schuur in Cape Town.

**What’s the problem?**

The questions being asked were whether routine full blood counts (FBC) on admission to a medical inpatient ward made sense. Historically 96% of patients had the test done, but how often did the results of the test influence management?

**Study**

For 165 consecutive admissions an FBC was requested, which included haemoglobin, white cell count, platelets, mean corpuscular volume and haematocrit. Results were made known to the registrar, but to the consultant only after she/he had completed a questionnaire. This included whether, after a history and examination, an FBC was needed for the medical management of the patient. The result was then made known and the consultant had to indicate whether the result influenced patient management.

In order to assess agreement between consultants, two independent consultants examined the results of the first 50 patients in the same way, relying on clinical notes to see if they agreed with the original decision.

**Results: top docs in kappa shock**

There was moderate agreement between consultants and independent assessment on whether tests were needed (kappa 0.49 – 0 is complete disagreement, 1 is complete agreement; see Bandolier 43). There was not much agreement, though, on whether the test assisted in patient care (kappa 0.06).

Consultants’ clinical judgement was good. When they had a high suspicion of abnormality on clinical grounds, the test was abnormal 80% of time. Where there was no clinical indication for an FBC, there was a low (2%) probability that the result would assist patient management. That 2% came from a single case, and there was disagreement even over that as to whether there was actually any real effect on patient management.

The bottom line was that 25% of FBCs ordered were unnecessary, and that avoiding them by changing policy could save Groote Schuur about £3,500 a year.

**Comment**

Small beer, to some extent. Groote Schuur is a big hospital, and £3,500 and a few tests saved doesn’t add up to much. But perhaps the main lessons lie elsewhere – in the excellent clinical skills of their consultants in judging when tests were
needed, but their inability to agree when results of tests affect patient management. This may be one of those abstruse definitional things, but lots of disagreement indicates an area where further evidence or work is needed.

At the very least, this paper gives an interesting exemplar of how any institution might begin to assess how to make the best use of its diagnostic test budgets. A rolling program starting with highest volume or cost tests would be educational. Are there other examples we should know of?

Reference:

IDENTIFYING HEAVY DRINKERS

A simple test to identify heavy drinkers, the CAGE test, was given in Bandolier 35. Four simple questions are asked:

- Have you ever felt you should Cut down on your drinking?
- Have people Annoyed you by criticising your drinking?
- Have you ever felt bad or Guilty about your drinking?
- Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (Eye-opener)?

Scores of 3 or 4 were highly suggestive of heavy drinking in a large teaching hospital medical outpatient population with a 36% prevalence [1]. So how do laboratory tests compare?

Modelling laboratory tests

A study in 426 heavy drinkers and 188 light drinkers evaluated the performance of 40 laboratory tests [2], with the patient population split into a training data set of 411 subjects and a validation set of 171. As well as the 40 common laboratory tests, three new tests (carbohydrate-deficient transferrin, haemoglobin-associated acetaldehyde and ß-hexosaminidase) designed to tell heavy from non-drinkers were tested. A number of diagnostic models found from systematic search of the literature were also examined.

Method

Strengths of association between a number of laboratory tests and true result were found and a model constructed called the heavy drinking index (HDI). A score of 0 on the HDI indicated a non-drinker, and 0.26 and above (up to 1) a heavy drinker.

Results

Ten laboratory tests were included in the final model. Not even the most significantly associated test (chloride) would be helpful alone though. Even though it had the highest odds ratio, the mean value of 104.1 in heavy drinkers was not so very different from the value of 102.5 found in light drinkers.

The HDI successfully separated heavy from light drinkers, with trivial overlap and a sensitivity of 98% and specificity of 95% (likelihood ratio 20). No other model of laboratory test came close to the efficiency of this, with one exception, though all were significantly associated with heavy drinking. The three new single tests had sensitivities of 40% or less at a specificity of 95% (likelihood ratio 8 at maximum).

Comment

This model was designed and tested in an unusual population, in which 69% of subjects were heavy drinkers. Would its efficiency be the same in a primary care population with a much lower prevalence of heavy drinking? And who, in primary care, would be able to run a complicated model like this?

The extraordinary cleverness of a model that does well in one particular setting is lost if it is unusable. Bandolier often wonders why a morning blood sample is simply not sent for an ethanol estimation. Simple, cheap, and with a CAGE score might well provide the ability to detect heavy drinking even when prevalence is low.

References:

DIAGNOSING PROSTHETIC JOINT INFECTION

Bandolier has complained about the poor quality of diagnostic test information in the past (Bandolier 61). A new study [1] laying out how to diagnose infection in a prosthetic joint at revision shows, par excellence, how to evaluate a diagnostic test.

In the UK we do over 75,000 hip and knee replacements a year. Some fail, and infection is one of the most serious causes of failure. Infection may present as pain in the joint and loosening of the prosthesis. Treatment may involve removing the joint and treating the infection locally and/or systemically before reimplanting another prosthesis. How best to treat chronic infections will depend on having an accurate and robust means of diagnosing infection.

The study

334 hip and knee revisions over a 17-month period were examined prospectively. The surgical teams were requested to send a standard set of five samples for culture and his-
Histology at the time of prosthesis removal. Details of the sampling of tissue and microbiological and histological testing are given in great detail, down to the use of different instruments and fresh scalpel blades to reduce risks of cross-contamination.

The results

Histology results were not available for all patients, so there was information on 297 joints (253 hip, 44 knee) for analysis, 41 of which were infected. Analysis showed (Table 1) that three or more specimens growing the same organism in microbiological tests was powerfully related to infection, with a likelihood ratio (LR) of 169.

Because the likelihood of infection was lower with prostheses which had been in situ for longer periods, the test results were applied to the number of years the prosthesis had been used (Table 2). This showed that even when the prosthesis had been present for more than 10 years and the pre-test probability of infection was as low as 6.6%, three or more positive specimens strongly predicted infection.

Histology with gram staining was shown to be a poor predictor of infection, with a likelihood ratio of 10.

Comment

As Mr Punch would say, “That’s the way to do it!” This is another classic paper demonstrating just how diagnostic strategies should be evaluated. Its value is not just for the diagnosis of infections in hip prostheses, but also as an exemplar for all of us when faced with a new or existing diagnostic test. If it can’t meet the standards laid out in this paper, why should we bother to use it?

The other very important aspect of this particular paper is that it is extraordinarily clear about how to reproduce the experimental situation in clinical practice. If, on reading this paper, you decided that you wanted to institute this as practice in your hospital, you could do it. It may be clever, but it is also practical, and full of common sense.

Reference:

**TUMOUR MARKERS AND CANCER TREATMENT**

It is often the case that the more important a paper, the harder it is to précis. That is certainly true of a fundamental exposition of the use of predictive and prognostic tests in cancer, and how they may be used to guide patient and doctor in choosing the correct, or any, adjuvant systemic therapy [1]. This paper is of massive importance to those using or producing tumour marker test results because it is likely to change the way you think.

**The problem**

I have a woman who has breast cancer. How do I know what her chances are of surviving the next 10 years? How do I know whether it is appropriate to treat her with systemic adjuvant therapy which might help her, but which has the certainty of some toxic effects that will harm her?

Are there any tests I can use that will tell me something about the likelihood of metastasis or growth rate of the cancer? If such a test existed, it would be a **prognostic** test.

Are there any tests associated with sensitivity and/or resistance to particular therapeutic agents? If such a test existed it would be a **predictive** test.

**TMUGS**

Not the easiest acronym to tip off the tongue, but the “Tumour Marker Utility Grading System” is one which has been defined by an expert panel of the American Society of Clinical Oncology. It uses a grading system from 0 to 3+, with 0 implying that sufficient data exist to say that a test is of no utility, while 2+ or 3+ implies that a marker should be considered or absolutely should be used.

The basis of these gradings is on levels of evidence, with the highest level being that of prospective, highly powered studies specifically addressing the issue of tumour marker utility. The lowest level of evidence is that where specimens happen to have been collected for a variety of reasons.

It won’t surprise thoughtful readers that most tests fall into a category with low levels of evidence which mean that their utility is uncertain. This means that most work done on most tumour markers is almost worthless. We may have highly valuable tools to assist decision-making in some tumour marker tests, but we just don’t know it.

**Strong/Weak**

This paper suggests a further extension of TMUGS into TMUGS-plus, in which the statistical associations found in reports on tumour markers is overturned in favour of clinical utility. This latter categorisation of strong, moderate or weak prognostic ability depends on how far a patient might be moved across prognostic borders - for instance if a positive or negative test moves a patient from a low risk of dying over 10 years to a high risk of dying.

Clearly, this is of immense clinical importance. It would mean, for instance, that while adjuvant treatment may not be sensible if the risk of death is low, it would be an absolute imperative if the risk of death was high and the chance of success moderate.

**The clever bit**

What makes this paper so important is that it shows us how to combine prognostic and predictive factors in ways that will help doctors and patients make decisions about therapy. They focus on pulling them together to produce a figure for the absolute reduction in mortality due to systemic therapy in patients for whom a marker is positive compared to those in whom a marker is negative.

The authors use a pre-determined set of recommendations for treatment. Thus if 10% or more of a group of patients being treated benefited (in this case lived for at least 10 years), then treatment would be absolutely recommended. If it was between 6% and 9% treatment would be probable, between 4% and 5% considered but not strongly recommended, and between 0% and 3% not recommended. These figures would be equivalent to NNTs of 10 or less, 11-17, 18-33 and more than 33.

**A new paradigm**

This paper may be one of the most important ever written on diagnostic tests, but it will never be an easy read, especially the first time. By the third of fourth time you will start to see that it opens up new horizons in the way that diagnostic tests are looked at, and the way in which tests and treatments can be combined together to produce real benefits for patients.

For cancer, it will help define what is acceptable in the evaluation of diagnostic tests. For cancer therapy, it will help define how clinical trials may be designed to demonstrate effectiveness. For new genetic tests which might have predictive or prognostic relevance it provides a framework which will allow their evaluation to be faster and more certain.

Any paper which says that a p value, even if very low, does not necessarily imply that a factor (test, result, whatever) is useful tells you that it has some thought behind it.

Taken together, this paper, and that on diagnosis of prostatic joint infection on page 5, form a primer on how to think about diagnostic testing. They are a “must read” for anyone working in laboratories and producing tests. They should be a “must teach” for those responsible for educating doctors and other health professionals. Bandolier is delighted to see them, and will continue to seek out other examples of excellence in diagnostic testing.

Reference:
LOW MOLECULAR WEIGHT HEPARIN
AND KNEE REPLACEMENT

Deep venous thrombosis (DVT) is a common postoperative complication of knee replacement, and is a common cause of re-admission. It can occur in the lower leg, or proximally in the popliteal vein. Proximal vein thrombus formation is associated with a small but finite risk of pulmonary embolism, and a small proportion of those affected will die.

Trying to prevent thrombus formation is often done prophylactically, and agents used may include warfarin or heparin. Low molecular weight heparin (LMW heparin) has been around for more than a decade now, and has theoretical advantages because of longer half-life and because it can be used at fixed doses subcutaneously without laboratory monitoring.

The question of what additional benefit, if any, obtains from the use of LMW heparin is answered by a meta-analysis of randomised trials [1].

Search

The search was comprehensive, and sought randomised trials in knee replacement of thromboprophylaxis with LMW heparin compared with placebo or active control in which routine screening for DVT was done.

Results

Ten studies were found; eight used an active pharmacological control, either standard heparin or warfarin. The other two used placebo. Four different makes of LMW heparin were used and the doses are given in the paper; for enoxaparin in five trials it was 30 mg twice daily or 40 mg once daily. The duration of the studies was 8 to 14 days or until discharge, and venograms were used to screen for DVTs in all cases.

♦ A DVT occurred in 506/2039 (25%) patients given LMW heparin and in 690/1884 (37%) of patients given control (Figure). The relative risk was 0.68 (95% confidence interval 0.62 to 0.75) and the number needed to treat to prevent one DVT was 8.5 (6.8 to 11).

♦ A proximal DVT occurred in 93/2039 (5%) patients given LMW heparin and in 166/1884 (9%) of patients given control (Figure). The relative risk was 0.52 (0.41 to 0.67) and the number needed to treat to prevent one proximal DVT was 24 (17 to 37).

♦ In nine trials for which there was information, a pulmonary embolus occurred in 4/1974 patients given LMW heparin and 9/1823 given control.

♦ In nine trials for which there was information, a bleeding complication occurred in 58/1863 (3.1%) of patients given LMW heparin and 45/1708 (2.6%) of those given control.
There were no deaths with LMW heparin in six trials, and three with control.

Comment

Argument might still rage about the use and possibly abuse of LMW heparin, but this paper will be useful in helping to resolve the issues. Be careful while reading it, as Bandolier found a few minor errors in some of the tables in the calculation of relative risk for individual trials. We used the total of patients randomised to give an intention to treat outcome for relative risk and NNT. The paper appears to use evaluated patients rather than all patients randomised.

The paper also shows us in sensitivity analyses that the type of control is not important, and that papers of poor reporting quality may give higher estimates of treatment effect (though it doesn’t actually give the quality scores).

That aside, this paper could easily be used to do some “back-of-stamp” health economics to evaluate whether the additional costs of LMW heparin repay themselves in other ways.

Reference:

Medical therapy for Pouchitis

A splendid systematic review [1] of four randomised trials in this rare chronic inflammatory disease in the ileal pouch after ileal pouch-anal anastomosis shows that metronidazole (NNT 1.6) and oral probiotic bacteria (NNT 1.2) are effective. Other treatments are not effective. The condition may be rare, but this shows how good systematic review methods can still help.

Reference:

Bandolier Conferences

Pain – where’s the evidence?

These two conferences will take place on July 6th and July 8th in London and Manchester respectively. In London the venue will be the Royal College of Pathologists in Carlton House Terrace near Trafalgar Square. In Manchester we have booked a conference suite in Terminal 2 at Manchester Airport – convenient for parking, for rail, and for anyone travelling from further afield by air. The meetings will start at about 9.30 am and will finish by 5.00 pm.

The themes of the meetings are the quality, validity and availability of evidence for the treatment of acute and chronic pain. The new Bandolier Oxford Pain Internet site will be unveiled. The preliminary programme includes the following:

- Pain – how big is the problem?
- Methods in pain reviews: quality and validity
- Acute pain – the evidence
- The Oxford Internet Pain Site
- Chronic pain – the evidence
- Arthritic pain – the evidence
- Adverse effects of NSAIDs
- Economic considerations
- Guideline developments – using the evidence

We hope to have additional information on evidence-based pain for nurses, and information on the Cochrane Collaboration group on Pain, Palliative and Supportive Care.

The meeting will be useful for those in primary and secondary care, for nurses and pharmacists as well as doctors. We have places for about 80 people for each venue, and the cost is a mere £50, and that includes a free paperback copy of the book “An evidence-based resource for pain relief”.

For more details please fax Eileen on 01865 226978, or write to her at the Bandolier address. If you want to book early, please send a cheque made out to Bandolier and tell us which venue you want and whether you have any special dietary requirements.

Posters

We would love to hear from anyone who has used evidence in pain relief to make a difference. Some people have asked in previous Bandolier conferences to put up posters. If you would like to, then please fax Anna Oldman on the Bandolier number.