Clinical opinions in general medicine

In 2001 College President Niall Finlayson suggested that *The Journal* introduce a new educational feature, Clinical Opinions. This section brings recently published papers of general interest to the attention of our Fellows, Collegiate Members and Associates. With increasing specialisation and sub-specialisation it is important, although difficult, for all physicians to keep abreast of developments outside their own area of expertise. In this, the first round of clinical opinions we present a variety of papers selected by specialists in clinical and laboratory medicine: Ryan reminds us that each patient should be treated as an individual, including their laboratory test results, and that 'normal' ranges are not always what they appear to be; Kearney highlights the fact that, in a world of increasing hospital acquired infection, the solution is literally in our hands – soap, water and alcohol wipes. Elsewhere we learn about an effective treatment for one type of lung cancer which, despite being superior to current chemotherapy regimes, is under-utilised. Anderson raises the uncomfortable possibility that this may be due to effective marketing of chemotherapeutic agents by drug companies. Further evidence that the Americans and the British are '2 peoples separated by a common language' comes from the *American Journal of Kidney Disease*. British GPs are much less likely to refer patients for dialysis than their transatlantic cousins and Brown suggests that hospital physicians can play an important role in identifying and referring patients for dialysis.

We hope you will find these papers interesting, informative and applicable to your general medical practice, irrespective of your specialist interest. We welcome comments related to specific papers and comments about our new feature in general. Correspondence may be sent by email to Calum Macleod, CME Editor (editorial@rcpe.ac.uk).

TITLE: Analytical performance characteristics should be judged against objective quality specifications.

KEYWORDS: Laboratory test, quality, specifications.

AUTHORS: Fraser CG, Petersen PH.

JOURNAL: *Clinical Chemistry* 1999; **45:**3, 321–3.

SUMMARY:
The performance of a test can be judged against a variety of standards; state of the art, expert views or biological variation. The generation and application of standard quality specifications are common subjects of discussion in the field of laboratory science. Ideally, quality specifications for test performance should be derived from an objective analysis of clinical needs. Unfortunately, tests are seldom used in well-defined, single clinical situations with standard, well-defined clinical strategies directly related to the test result. In routine practice, test performance assessed analytically may bear no relationship to actual clinical need.

OPINION:
Clinicians are constantly exposed to publications extolling the virtue of some new laboratory test. Few are equipped to judge the analytical and methodological aspects of the paper. This commentary provides the non-specialist with a useful insight into the area of laboratory quality testing and briefly describes a variety of standards against which performance can be judged. Of particular relevance to clinicians is the section dealing with the concept of biological variation and the effect of such variation on laboratory test result interpretation. This should be compulsory reading for any clinician dealing with laboratory test results and attempting to relate such results to so-called 'normal' ranges. Clinicians should begin to familiarise themselves with these concepts that have previously been the preserve of their laboratory colleagues.

Dr Michael Ryan

TITLE: The laboratory diagnosis of urinary tract infection.

KEYWORDS: Laboratory diagnosis, urinary tract infection.

AUTHORS: Graham JC, Galloway A.

JOURNAL: *Journal of Clinical Pathology* 2000 **54:**911-19.

SUMMARY:
Urinary tract infection (UTI) is common and it is not surprising that urine specimens make up a large proportion of those samples submitted to the routine diagnostic laboratory. Many of the samples will show no evidence of infection and most laboratories will attempt to screen these out at an early stage. Those samples with evidence of infection need to have the degree of bacteriuria accurately quantified and linked to clinical relevance. The authors highlight the limitations of reagent strip screening and common misperceptions about the interpretation of urine bacteria counts. They suggest there is a need to examine both the cost effectiveness of the way urine samples are processed and the evidence base for the final report on which important clinical decisions may depend.

OPINION:
Urine samples make up the largest proportion of the specimen workload received by a service laboratory; 200–300 samples per day for a large laboratory. Consequently, laboratories use a 'screening' method and are unable to approach each specimen individually. Reagent strip testing is limited as a screening tool by the occurrence of both false-positive and false-negative results and is not recommended in children. Clinicians should be aware of the limitations of the screening method used by their local laboratory and may wish to request more extensive culture in specific cases. Culture remains the gold standard with a colony count of $>10^5$ organisms per ml being considered diagnostic. However, this paper reminds us that purity of culture is a more accurate indicator of infection as low bacterial counts can occur in UTI for a variety of reasons; urinary frequency, excessive hydration and haematogenous infection of the urinary tract. It is worth remembering that for low counts of a pure growth the reliability of culture in diagnosing UTI is increased from 80% in a single positive culture to 90% if a repeat shows identical results. This paper is recommended to all clinicians who interpret laboratory urine results.

Dr Patricia Kearney

TITLE: Contamination of gowns, gloves and stethoscopes with vancomycin-resistant enterococci.

KEYWORDS: Contamination, gowns, gloves, stethoscopes.

AUTHORS: Zachary KC, Boyne PS, Morrison VJ *et al.*

JOURNAL: *Infection Control and Hospital Epidemiology* 2001; **22:**560-4.

SUMMARY:
This study set out to measure the rate of contamination, during routine patient examination, of gowns, gloves and stethoscopes with vancomycin-resistant enterococci (VRE). Forty-nine patients colonised or infected with VRE were entered into the study between January 1997 and December 1998. Vancomycin-resistant enterococci were isolated from at least one examiner site in 67% of cases. Gloves were contaminated most commonly (63%), followed by gowns (37%) and stethoscopes (31%). In 24% of cases all three items were tested positive VRE. Only one out of 49 stethoscopes was positive for VRE after wiping with an alcohol swab. Contamination at any site was more common if the patient had a colostomy or ileostomy.

OPINION:
The authors have provided objective evidence of a high (67%) rate of contamination of gloves, gowns and stethoscopes during routine examination of patients colonised or infected with VRE. The methodology was scientifically sound and it is noteworthy that enrichment culture was not used, thus accurately mimicking the *in vivo* contact of a hand or glove with contaminated skin. Importantly, the effectiveness of decontaminating the head of a stethoscope with an alcohol wipe has been confirmed. There appeared to be no difference between contamination rates arising from examination of a colonised or infected patient.

This highlights the potential for spreading hospital acquired pathogenic organisms from unidentified, asymptomatic colonised patients. Screening of all patients for such organisms is costly, impractical and unlikely to result in lower transmission rates. The transmission of such organisms can be prevented, as this paper shows, by simple low-tech interventions. Washing one's hands, decontaminating of stethoscopes and appropriate use and disposal of protective clothing should be an integral part of everyone's clinical practice for each patient on every occasion.

Dr Patricia Kearney

TITLE: Continuous Hyperfractionated Accelerated Radiotherapy (CHART) versus conventional radiotherapy in non-small-cell lung cancer: a randomised multicentre trial.

KEYWORDS: Non-small-cell lung cancer, radiotherapy.

AUTHORS: Saunders M, Dische S, Barrett A *et al.*

JOURNAL: *Lancet* 1997; **350(9072):**161-5.

SUMMARY:

This study included 563 patients with locally advanced inoperable non-small-cell lung cancer (NSCLC) and a performance status of 0 or 1. Patients were randomly allocated to CHART (36 fractions in 12 consecutive days) or conventional radiotherapy (30 fractions in six weeks). For those receiving CHART there was a 24% reduction in the relative risk of death, equivalent to an absolute improvement in two year survival of 9% from 20% to 29% (p = 0·004, 95% CI 0·63–0·92). During the first three months, severe dysphagia occurred more often in the CHART group than in the conventional radiotherapy group (19% vs. 3%). Otherwise there were no important differences in morbidity.

OPINION:

These results were originally published in 1997 and dated in 1999 (*Radiotherapy and Oncology* 1999; **52(2):**137-48). CHART offers a significant survival benefit over conventional treatment for a large subgroup of patients with inoperable but localised NSCLC. The survival benefit has not been disputed in the literature, yet CHART is not widely available. There are logistical difficulties in providing CHART, which involves treatment out of hours. Nevertheless, the cost of this treatment is less than some forms of chemotherapy which are available and offer less benefit. Clearly, radiotherapy does not benefit from many of the marketing advantages offered by drug companies.

Dr Wendy Anderson

TITLE: End-stage renal disease: Factors affecting referral decisions by family physicians in Canada, the United States and Britain.

KEYWORDS: Dialysis, family physicians, referral decisions.

AUTHORS: Wilson R, Godwin M, Seguin R *et al.*

JOURNAL: *American Journal of Kidney Diseases* 2001; **38(1):** 42-8.

SUMMARY:

Acceptance rates for dialysis vary greatly between countries. This study sought to determine which factors influence referral by family physicians to a nephrologist. Almost 6,000 family physicians in three countries were surveyed and supplied with a clinical vignette. The response rate was 37%. The influence of patient age on referral practice differed; 51% of British physicians used age (mean age 82 years) as a criterion for referral compared with only 35% of North American physicians (mean age 85 years). The influence of renal function on referral patterns varied, with British physicians referring at lower serum creatinine levels (260 umol/l) than North American physicians (307 umol/l). Overall, however, British physicians were less likely to refer than their transatlantic counterparts. Younger physicians were more likely to refer than their older colleagues.

OPINION:
The number of patients with end-stage renal disease continues to grow. However, a considerable number of patients do not see a nephrologist until late in their disease process. Patients referred early can be better prepared for dialysis, have an A-V fistula created and undergo multidisciplinary assessment. This study shows that many family physicians do not refer early and would not refer, at al1, some patients who would clearly benefit from dialysis. Most nephrologists would recommend referral when serum creatinine reaches 150–200 umol/l. Acceptance rates are much lower in the UK than North America and this may be due in part to referral practices. Although resource limitations would not currently permit treatment rates in the UK anywhere close to those in North America, it seems inappropriate for family physicians to act as the sole gatekeeper to dialysis services. Hospital physicians have an important role to play in identifying those patients who might benefit from early referral to a nephrologist, and this paper illustrates why.

Dr Henry Brown

TITLE: Dose-response relation of inhaled fluticasone propionate in adolescents and adults with asthma: meta-analysis.

KEYWORDS: Asthma, inhaled steroids, fluticasone.

AUTHORS: Holt S, Suder A, Wetherall M *et al.*

JOURNAL: *British Medical Journal* 2001; **323:**253-6.

SUMMARY:
A meta-analysis of placebo controlled, randomised clinical trials that presented data on at least one outcome measure of asthma and that used at least two different doses of fluticasone. Eight studies with 2,324 patients with asthma met the inclusion criteria. It was concluded that in asthmatics most of the therapeutic benefit of inhaled fluticasone is achieved with a total daily dose of 100–250 μg, and the maximum effect is achieved with a dose of around 500 μg/day. It was noted that there were few dose response studies that included doses of >500 μg/day.

OPINION:
Inhaled corticosteroids are the most effective anti-inflammatory drugs for treating asthma and have revolutionised the management of asthma since their introduction in the early 1960s. National guidelines allow maximum dosages of Beclometasone and Budesonide of 2,000 μg/day, but the more potent fluticasone is licensed for use up to 2000 μg/day in adults. It is not unusual in primary and secondary care to prescribe such high doses of inhaled steroids in more severe asthmatics. However, it is clear that published data does not support a dose response relation of inhaled fluticasone at doses >500 μg/day. The risk benefit ratio of inhaled steroids is most favourable at lower doses. Use of higher doses (>fluticasone 500 μg/day or >1,000 μg/day Budesonide or Beclometasone) may not be any more effective and are associated with an increasing risk of systemic side-effects, especially with more lipophilic steroids such as fluticasone. Physicians should consider other alternatives first when asthma remains uncontrolled with a moderate dosage of inhaled steroids, e.g. improving compliance, improving inhaler technique, addition of long acting inhaled bronchodilators or leucotrine receptor antagonist. Subsequently, any further increase in inhaled steroid should be on a trial basis, reviewed closely and reduced to the minimum effective dosage if there is no objective benefit.

Dr Geoff Todd

TITLE: Systemic review of clinical effectiveness of pressurised metered dose of inhaler versus other hand held inhaler devices for delivering corticosteroids in asthma.

KEYWORDS: Meter dose inhalers, asthma, inhaled corticosteroids.

AUTHORS: Brocklebank D, Wright J, Cates C. (National Health Technology Assessment Inhaler Review Group, UK)

JOURNAL: *British Medical Journal* 2001; **323:**896-900.

SUMMARY:
A systematic review of randomised controlled trials to determine the clinical effectiveness of pressurised metered dose inhalers compared with other hand held inhaler devices for the delivery of corticosteroids in stable asthma. Twenty-four randomised controlled trials were included. Significant differences were found for FEV1, PEFR and use of drugs for additional relief with dry powder inhalers. However, for various reasons the authors dismissed these findings, e.g. 'the method of data analysis used in all 3 was potentially biased in favour of the dry powder inhaler groups'. They concluded that 'no evidence was found that alternative inhaler devices are more effective than the pressurised meter dose inhalers for delivery of inhaled corticosteroids. Pressurised meter dose inhalers remain the most effective first line delivery devices'.

OPINION:
Pressurised metered dose inhalers are the cheapest and most frequently prescribed inhaling devices. The authors failed to highlight in their paper the difficulties most patients have with using these devices, even with the addition of a spacing device, which many patients find too bulky to carry around (although the smaller Aerochamber is more acceptable). The paper is controversial and their interpretation of comparative studies with other inhaling devices has been criticised in subsequent correspondence. Nonetheless, for those patients with good, consistent technique, this paper reminds us that this most durable of devices should probably remain the first line choice in stable, mild to moderate, asthmatics.

Dr Geoff Todd