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Risk, safety, and the dark side of quality

Improving quality in health care should include removing the causes of harm

Clinical risk management was initially considered a means of controlling medical negligence litigation. Gradually, however, the need systematically to examine the underlying clinical problems became apparent, together with the need to care for injured patients rather than simply treating them as potential litigants.[1] Though driven by anxiety about litigation, risk management has the potential to act as a gateway into a more important problem, which current quality initiatives have not adequately addressed: injury to patients.

Can care that is actually harmful be encompassed in traditional frameworks of quality, such as Maxwell's dimensions of effectiveness, efficiency, appropriateness, acceptability, access, and equity?[2] Certainly harmful treatment will be ineffective, inappropriate, and unacceptable but these terms imply an absence of quality rather than actual danger or harm. Maxwell's dimensions are important, but, in the positive way they have been interpreted, have perhaps directed attention away from quality's darker side.

Iatrogenic effects of drugs and other treatments have been recorded in many studies, but only recently has the scale of injury to patients become apparent. The Harvard study found that patients were unintentionally harmed by treatment in almost 4% of admissions in New York state. For 70% of patients the resulting disability was slight or temporary, but in 7% it was permanent and 14% of patients died partly as a result of their treatment.[3] Serious harm therefore came to about 1% of patients admitted to hospital. Similar findings were reported from Colorado and Utah in 1992 (personal commuication, T Brennan). A recent Australian study revealed that 16.6% of admissions resulted in an adverse event, of which half were considered preventable.[4] Extrapolating from these figures to a hospital with 50 000 admissions a year suggests 2000-8000 adverse events a year leading either to injury or to a longer hospital stay.

The cost of litigation in Britain has been estimated at £100m to £150m a year,[1] now probably nearer £200m. This is about 0.5% of the NHS budget and could be viewed simply as an insurance problem. The calculations look different, however, when the real costs of adverse events are considered, as these vastly outweigh the costs of litigation. An operation with an adverse outcome may lead to further operations, a longer stay in hospital, additional outpatient appointments, and so on. In Australia adverse events were estimated to account for 8% of all hospital bed days.[4] Disability payments and other benefits probably far outweigh the costs of individual hospitals. Adverse events also involve a huge personal cost to the people involved, both patients and staff.[1]

Recent research in medicine and elsewhere suggests actions that should be taken to improve safety. Firstly, the dictum of first doing no harm needs to be taken seriously.[5 6] No treatment is risk free, but safety should at least be recognised as the first dimension of quality. An airline that functioned in the manner of the hospitals in the Harvard study could be generally effective, efficient, and so on, save for the 1% of journeys in which passengers were seriously injured.

Potential for error must be acknowledged

Secondly, the potential for error in medicine needs to be openly acknowledged. Skilled and routine tasks can be carried out reliably, but the probability of error and biased decision making increases greatly in novel situations as the limits of the brain's information processing capacity are reached. At times of stress and uncertainty the probability of mistakes inevitably increases, no matter how conscientious the clinician.[7] Nevertheless, in medicine fault free performance is expected always. Error prevention involves exhortation, training, or disciplinary measures directed at the individual.[6] But people do not intend to make errors and it is often pointless to chastise them for doing so.

Thirdly, analyses of accidents in medicine and elsewhere have led to a broader understanding of accident causation, with less focus on individuals and more on organisational factors that provide the conditions in which errors occur.[8] In medicine the root causes of adverse events may lie in factors such as communication and supervision, workload, educational and training deficiencies, the use of locums, and so on. The same organisational problems, such as poor communication within a team, may lead to a wide variety of adverse clinical events. After serious incidents the first question should be, "What does this tell us about our system?" and only then, "What does this tell us about this individual?"[9]

Fourthly, targets for audit, clinical effectiveness programmes, and other quality initiatives should be explicitly selected from areas where patients are at high risk. The American and Australian studies show that high rates of preventable adverse events (20-30%), and of resulting permanent disability, occurred during

treatment for infectious diseases, injuries, and poisonings and from the toxic effects of drugs.[4]

Fifthly, the fact that risk management is generally centred on single adverse events may bring a new richness to the analysis of the quality of health care. Practitioners of audit know that "counting is not enough,"[10] in that descriptive data do not necessarily reveal the underlying problems, and some argue that successful audits are those that specifically analyse underlying causes.[11] Critical incident and organisational analyses of individual cases have illustrated the complexity of the chain of events leading to an adverse outcome.[12-14] Finally, clinical risk management should aim at more than avoiding litigation and must be integrated with clinical audit and other quality assurance activities.

A healthcare safety programme

What might a safety programme in health care look like? In industry such programmes target the tasks, teams, and conditions of work rather than the staff.[8] Safety needs to be tackled both at the level of the particular clinical process, as in clinical audit, and at interpersonal and organisational levels. Audits need to be supplemented by broader analyses of organisational and system features. When tasks can be clearly specified greater standardisation, clear guidelines, and less reliance on human memory and vigilance are essential. Team and communication failures have been strongly implicated in many accidents and remedial measures can be cheap and straightforward. Systems have also been developed in industry to monitor the conditions of work and the associated organisational factors and decisions that may predispose to risk and unsafe practice.

Systemic change, at both clinical and organisational levels, involves a commitment to safety and quality at all levels of an organisation, a fact long recognised by proponents of total quality management. The examination of individual incidents in a risk management programme is a powerful way of examining the factors implicated when things go wrong, but thoroughgoing change will require a range of quality and safety techniques embedded in a comprehensive strategy. If the true costs of adverse events are recognised, rather than the comparatively trivial costs of litigation, then resources may be made available to implement the comprehensive strategies needed.

The responsibility for adverse events rests not always with the unfortunate junior nurse or doctor caught in the crossfire but also with those taking higher level organisational decisions affecting the conditions of work; these might be senior clinicians, hospital management, the purchasing authorities, and even the secretary of state for health. From this perspective litigation can be seen not simply as a threat but as a way of revealing unsafe conditions of practice and putting pressure on those with the authority to implement change. Interesting times would indeed be ahead if lawyers sued those they perceived as truly responsible for adverse events, rather than the staff with immediate responsibility for the care of the injured patient.

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Treating diarrhoea

Severe community acquired diarrhoea calls for an antimicrobial drug, preferably a quinolone

Diarrhoea is a great equaliser. It afflicts all ranks, young and old, hale and infirm, with symptoms that range from mild discomfort to life threatening dehydration. The British Society for the Study of Infection recently published a helpful consensus statement on the management of infective gastroenteritis in adults.[1] It provides a concise yet comprehensive account of diagnosis and treatment with fluid replacement, antidiarrhoeal agents, and antimicrobial drugs, especially the quinolones.

Since a consensus statement is, by definition, a compromise between the individual opinions of experts, such declarations, particularly those concerning treatment, tend to be rather conservative. It is easier to find disagreement among the assembled experts than universal acceptance of a specific treatment. As an individual commentator I have licence to express more bold opinions than those of the consensus statement, which are rather cautious concerning treatment.

My approach to treatment is based on two premises. Firstly, a person who is sufficiently ill with acute diarrhoea to seek medical attention wants to receive treatment that will provide prompt relief.

Secondly, safe and effective drugs are available to provide prompt relief of acute gastroenteritis that causes unremitting call to stool.

In order to choose the appropriate drug, it is necessary to stratify the severity of illness. For mild to moderate diarrhoea, with three or fewer bowel motions a day, bismuth subsalicylate (PeptoBismol) can give excellent relief with virtually no side effects, except for blackening of the tongue and stool. Bismuth subsalicylate is an insoluble complex of trivalent bismuth and salicylate. The drug possesses antimicrobial activities on the basis of the bismuth and antisecretory properties related to the salicylate moiety.[2] In the four therapeutic trials of travellers' diarrhoea conducted in Mexico and west Africa, bismuth subsalicylate reduced frequency of diarrhoea significantly more than placebo, but results were generally better with the higher dose (4.2 g a day).[3]

For greater effectiveness when the diarrhoea is more severe (up to four loose motions a day), an antimotility drug is the best choice. Loperamide induces rapid improvement, demonstrable even on the first day of treatment, when the results were significantly better than either placebo or bismuth subsalicylate.[4]

The consensus statement raised the familiar canard that these agents "have been shown to be dangerous in shigellosis" based on a single report of adverse effects in a study of shigellosis in volunteers. This concern has largely been dispelled by clinical experience. Patients with shigellosis, even a patient with *S dysenteriae* type I, have been treated inadvertently with loperamide as the only drug, and the condition resolved without prolonging the illness or delaying excretion of the pathogen.[5-7] Certainly, the antimotility drugs should not be given to any patient with diagnosed shigellosis or with dysentery (bloody, mucoid stools and fever), which is commonly seen in developing countries or in returning travellers. However, this concern about shigellosis should not discourage the use of the antimotility drugs for mild to moderate diarrhoea in community practice. Indeed, the overall safety record of loperamide is so good that it is sold over the counter in many countries.

Now the vexing issue of treatment with antimicrobial drugs. The matter has become more contentious with the recent publication of a study of empirical treatment of severe, acute community acquired gastroenteritis with the quinolone antibiotic, ciprofloxacin.[8] This is the fourth study with similar design and, with slight variations, similar conclusions.[9-11] The British study by Dryden *et al* included patients with more than four fluid stools a day for more than three days who had at least one associated symptom.[8] They were treated with either ciprofloxacin 500 mg twice daily or placebo for five days. As in the other studies, the authors observed a reduction in diarrhoea and other symptoms after about two days, with fewer treatment failures, and significantly greater clearing of pathogens when compared with placebo. Six weeks later there was no difference in stool carriage of the pathogen (12%), and no demonstrable antibiotic resistance emerged during treatment.

I conclude from these studies that patients with severe community acquired diarrhoea, defined as more than four loose motions a day and an associated symptom, should receive an antimicrobial drug, preferably a quinolone. In this subset of patients with acute diarrhoea, there is a high likelihood of isolating a bacterial pathogen (87% in Dryden *et al*'s study[7]), and the antibiotic provided prompt relief with a low risk of adverse effects.

All of the aforementioned studies relate to adults with diarrhoea. Readers should be cautious about applying these recommendations directly to children with diarrhoea. Some authorities recommend quinolones in developing countries, where severe diarrhoea in children is life threatening, but this is controversial because of potential toxicity in this age group.

In the treatment of adults some questions remain—the choice of drug, the dose, and the duration of treatment. Most studies have used ciprofloxacin 500 mg twice daily for five days, yet a recent study of travellers' diarrhoea used a single 500 mg dose of ciprofloxacin with good results.[12] My view is that five days is too long, especially when many patients will have substantial relief within 24 hours. A ploy to reduce duration of symptoms even more is to combine an antimotility drug with an antimicrobial, which has proved highly effective in some, but not all, studies.[13]

So how long must a patient suffer before being given the antibiotic? Most studies require at least three days of symptoms before patients are eligible. But Wistrom and Norrby found that patients who were treated within 48 hours of onset of diarrhoea had a much better result from norfloxacin treatment that those treated later in their course.[11] Whatever the choice of treatment for acute diarrhoea, it should be started at the initial visit to the doctor.

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Chlamydia pneumoniae and coronary heart disease

Coincidence, association, or causation?

Established cardiovascular risk factors such as cigarette smoking, diabetes mellitus, hypertension, and hypercholesterolaemia do not fully explain the temporal and geographical variations in the prevalence of coronary heart disease over the past century. Clinical data and animal models suggest that common chronic infections (including cytomegalovirus, herpesviruses, *Helicobacter pylori*, and dental sepsis) may also contribute to the pathogenesis of atherosclerosis.[1] However, the evidence that these infections can directly cause atherosclerosis is inconclusive.

Much stronger evidence now exists linking *Chlamydia pneumoniae*, an obligate intracellular pathogen, with coronary heart disease. This organism is a common cause of respiratory tract infections, which are usually subclinical and self limiting. Since *C pneumoniae* is difficult to culture, confirmation of infection often requires identifying systemic antibody responses. About half of the population is seropositive to *C pneumoniae* by the age of 50 years, suggesting that reinfection is common.[2]

Several recent studies have shown an association between antibodies to *C pneumoniae* and coronary heart disease.[3-6] In 1988 investigators in Finland showed that patients with acute myocardial infarction and known chronic coronary heart disease had significantly elevated antibody titres against *C pneumoniae* compared with healthy controls.[3] These researchers also showed prospectively that patients in the Helsinki heart study who had elevated IgA titres against *C pneumoniae*, or the presence of immune complexes containing *C pneumoniae* antigen, were twice as likely to suffer a cardiac event within the following six months (odds ratio 2.3, 95% confidence interval 1.3 to 5.2).[4] This increased risk was independent of age, hypertension, and smoking status. Other workers have corroborated the association between titre and prevalence of coronary heart disease.[5 6]

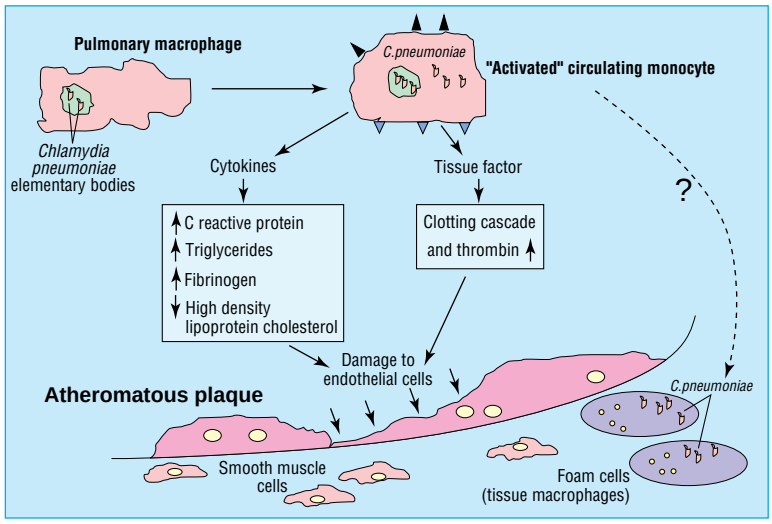
Such seroepidemiological studies can be criticised with regards to the selection of control patients; the titres of antibodies to *C pneumoniae* empirically chosen to indicate seropositivity; and the uncertainty as to whether an elevated antibody titre indicates active infection with *C pneumoniae*, past infection, or is just a reflection of antigenic cross reactivity.

Examination of plaques from coronary[7 8] and other arteries[9] (using both immunohistochemical and polymerase chain reaction techniques) has provided more direct evidence of possible involvement of *C pneumoniae* in atherosclerotic disease. In one study of coronary artery specimens at necropsy the organism was identified within macrophages, which make up the lipid rich core of plaques, and in smooth muscle cells, but not in normal tissue adjacent to the sclerotic lesions nor in control normal arteries.[7] In another investigation *C pneumoniae* was detected in 71 of 90 (79%) coronary atherectomy specimens from patients with angina but in only one of 24 (4%) samples from patients without atherosclerosis.[8]

How *C pneumoniae* enters atheromatous plagues and whether its presence reflects pathogenetic involvement in atherogenesis are not known. Macrophages may ingest particles of *C pneumoniae* in the lungs or elsewhere before migrating to the atheromatous lesion. *C pneumoniae* may simply reside in such macrophages without causing harmful effects, such that the association of the organism's presence and atherosclerosis is purely coincidental.

Alternatively, *C pneumoniae* is a plausible candidate for triggering and perpetuating inflammatory changes that contribute to the development of atherosclerosis. Chronic infection of macrophages with injury to blood vessels may be analogous to the pathogenesis of trachoma. In this case the closely related organism, *Chlamydia trachomatis*, causes scarring of the eye and blindness many years after the original infection, which is characterised by conjunctival infiltration with macrophages and lymphocytes.[10] Infection with *C pneumoniae* might induce a chronic immune activation, mediated by cytokines, that contributes to direct, chronic endothelial cell damage or stimulates the synthesis of acute phase reactants such as fibrinogen[11] and C reactive protein.[12] Chronic infection might also increase expression of monocyte derived procoagulants such as tissue factor[13] and thereby increase the risk of local or distant thrombosis.

The biological properties of *C pneumoniae* make it a potential culprit for initiating or modulating plaque formation. Like peptic ulceration related to infection with *Helicobacter pylori*, atherosclerosis may be a chronic inflammatory condition with a treatable infective cause. Preliminary evidence suggests that elevated antibody titres to *C pneumoniae* may be an independent predictor of outcome in men who have had a myocardial infarction. Furthermore, data suggest that in such patients antibiotic treatment reduces serum and monocyte activation markers[14] and is



Possible mechanisms for the involvement of *C pneumoniae* in atherogenesis

associated with a reduced likelihood of further cardiovascular events.[15]

Laboratory, seroepidemiological, and pathological evidence is accumulating for an association between *C pneumoniae* and coronary heart disease, but whether the organism is directly causal remains unclear. Establishing that such a widespread infection contributes substantially to the development of coronary heart disease will require further investigation; infection with *C pneumoniae* could turn out to be an important risk factor in certain individuals and to have complex interactions with conventional atherogenic risk factors. Large, prospective eradication trials with antichlamydial antibiotics, currently being designed, will help to finally clarify what role *C pneumoniae* plays in coronary artery disease.

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Screening for people with a family history of colorectal cancer

Target invasive screening to younger people with truly high risk

People with one or more first degree relatives affected by colorectal cancer have an increased risk of developing the disease themselves,[1-3] especially if a relative was affected at an early age (before age 45).[2 3] The excess risk is even more marked if the unaffected person reports a family history when aged less than 45.[1]. Hence, many centres offer colonoscopy every three years or even more frequently to people fulfilling the following criteria: one first degree relative affected by colorectal cancer before the age of 45; two affected first degree relatives; evidence of dominant familial cancer trait including colorectal, uterine, and other cancers. However, in practice even less restrictive criteria are employed. We wish to highlight some concerns about targeting invasive screening using criteria based on family history and to encourage further debate on this issue.

About 10% of patients with colorectal cancer have one or more first degree relatives who are affected.[2 3] People with a family history are twice as likely as the general population to develop colorectal cancer themselves,[1-3] but there is considerable variation in the risk to each person.[1 2] People from families with hereditary non-polyposis colorectal cancer (HNPCC) represent the high end of the risk spectrum. The lifetime risk of colorectal cancer for carriers of the gene is 80%.[4] Therefore, anyone belonging to such a family has, without genetic testing, an average risk of cancer of 40%. Colonoscopy provides survival benefit in these families,[5] but a screening interval of 12-18 months is essential.[6 7] However, recognition of affected families is confounded by lack of pathognomonic features, deficiencies in family information, adoption, early death of relatives due to unrelated causes, and incomplete gene penetrance. The result is that an appreciable proportion of gene carriers do not have sufficient affected relatives to meet faily history criteria for colonoscopy.[8] Hence, people with a very high risk of colorectal cancer are not well served by the use of criteria based on family history as a systematic approach to screening.

About 0.4% of the population have two first degree relatives affected by colorectal cancer,[1-3] representing 105 900 people aged 30-70 in the United Kingdom. Assuming a conservative estimate of four first degree relatives for each patient aged under 45 who presents with colorectal cancer annually in the United Kingdom, we estimate that a further 128 800 relatives fulfill the criteria. With a three yearly screening interval, an extra 78 233 colonoscopies would potentially be required annually at a cost of £11.7m. The resources required are of similar size to those for population screening by faecal occult blood test. We estimate the positive predictive value for identifying

Table Risk of colorectal cancer and of complications from colonoscopy over the next 10 years for people at various ages

Cumulative risks over next 10 years	Person's current age (years)			
	30	40	50	60
Risk of colorectal cancer in general population*	1 in 3038	1 in 603	1 in 174	1 in 73
Risk of colorectal cancer in people with positive family history†	1 in 506	1 in 101	1 in 87	1 in 36
Risk of death from colorectal cancer in people with positive family history†	1 in 843	1 in 168	1 in 145	1 in 60
Chance of colonoscopy preventing death‡	1 in 1054	1 in 210	1 in 181	1 in 75
Risk of serious complication from colonoscopy§	1 in 92	1 in 92	1 in 92	1 in 92
Risk of colonoscopy related death§	1 in 3077	1 in 3077	1 in 3077	1 in 3077

*Data from British population statistics and cancer registry data for 1990.
†Criteria for a positive family history are one first degree relative affected at age <45 years or two first degree relatives affected at any age. A sixfold increase in risk is calculated for people aged 30-49 and a twofold increase in risk for people aged 50-69.[1-3]
‡Assuming colonoscopy 80% effective in preventing cancer related death.[10]
§Assumes uniform risk of complications for all age groups, although risk of death probably increases greatly with age: one serious complication (perforation or major haemorrhage) per 300 colonoscopies and one death per 10 000 colonoscopies[10]; average of 3.25 colonoscopies in 10 years (three yearly screening intervals).

cancer at each colonoscopy based on family history criteria to be about 0.32%. This compares poorly with that for faecal occult blood test at 9.9%.[9] The United Kingdom National Screening Committee recently convened a series of workshops to determine whether mass population screening by faecal occult blood test merits implementation in the NHS. This structured approach to considering the case for population screening contrasts with the ad hoc implementation of screening for people whose only risk factor relates to their family history.

Focus on cumulative absolute risks

When offering advice to an individual patient regarding the balance of risk and benefit of screening, it is essential to focus on the cumulative absolute risk of cancer in the coming years compared to the cumulative risk of complications from colonoscopy. We have calculated the cumulative risk for the next 10 years of developing and dying from colorectal cancer compared to the risk of complications related to colonoscopy[10] for people aged 30, 40, 50, and 60 with two affected first degree relatives or one first degree relative affected under the age of 45 (table). Even though the relative risk of colorectal cancer is high (increased six fold), colonoscopy for people aged 30-49 with a family history is only six times more likely to save them from cancer than it is to kill them from colonoscopy. In addition, screening is considerably more likely to cause a serious complication in all age groups except the group aged 60-69 years. These risk comparisons are in stark contrast to those for a 30 year old male carrier of the gene for hereditary non-polyposis colorectal cancer, for whom we previously reported about a 1 in 1.7 chance of developing cancer by age 49.[4] This underscores the variation in absolute risk among people with a family history and the real need to systematically identify people from affected by hereditary non-polyposis colorectal cancer.

It is clear that invasive screening should be reserved for people with a substantial absolute risk of colorectal cancer.[7] Systematic case finding of gene carriers by mutation analysis is feasible[4] and could now be considered as an efficient approach to screening for people with greatly elevated risk of cancer. This would allow targeting of colonoscopy to people who would gain most from it. When information about gene mutation is not available, enrolment into colonoscopic screening programmes on the basis of family history should be through properly resourced clinical genetics departments to ensure accurate risk assessment and attention to counselling. The balance of risk to benefit means that colonoscopy on the basis of family history should be reserved for people from families with many affected relatives (three or more) showing a dominant mode of inheritance and early onset. People with a family history but who are not from families with hereditary non-polyposis colorectal cancer should be offered non-invasive screening such as faecal occult blood tests at about age 40.[10] Programmes raising pubic awareness of family history or encouraging general practitioners and hospital physicians to be proactive in identifying familial cases should be carefully evaluated since there is potential for raising anxiety among a large group who have only marginally increased risk.

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