CORRESPONDENCE

Long-term results of RITA-1

Sir—The summary of the latest publication of the RITA-1 trial (Oct 31, p 1419)[1] is misleading. Robert Henderson and colleagues say "initial strategies of PTCA [percutaneous transluminal coronary angioplasty] and CABG [coronary-artery bypass grafting] lead to similar long-term results in terms of survival and avoidance of myocardial infarction and to similar long term health care costs".

We construe this statement to indicate that the investigators interpreted their data to show that myocardial infarction is reduced or prevented by either intervention. There are no published data to support this belief—quite the opposite. The earlier randomised trials of surgery versus medical therapy showed no effect on the rate of myocardial infarction, and the two small randomised trials of PTCA versus medical therapy[2,3] showed a non-significant increase in myocardial infarction. Registry data also show that the risk of recurrent infarction is not improved by angioplasty—even if symptoms are.[4,5]

To perpetuate the myth that targeted intervention to one or more stenosed epicardial coronary arteries reduces the likelihood of infarction, is wrong. Most cases of myocardial infarction occur after thrombotic occlusion of arteries with less than 50% stenosis, and these arteries are the ones that are not selected for intervention. In this era of evidence-based practice, we are surprised that the investigators or indeed the reviewers have allowed this unsubstantiated statement to feature in this important report.

K S Channer, K M English

Department of Cardiology, Royal Hallamshire Hospital, Sheffield S10 2JF, UK

1 Henderson RA, Pocock SJ, Sharp SJ, et al. Long-term results of RITA-1 trial: clinical and cost comparisons of coronary angioplasty and coronary-artery bypass grafting. *Lancet* 1998; **352:** 1419–25.
2 Parisi AF, Folland ED, Hartigan PA. Comparison of angioplasty with medical therapy in the treatment of single vessel coronary artery disease. *N Engl J Med* 1992; **326:** 10–16.
3 Hueb WA, Belotti G, de Oliveira SA, et al. The medicine, angioplasty or surgery study (MASS): a prospective randomised trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenosis. *J Am Coll Cardiol* 1995; **26:** 1600–05.
4 Rouleau JL, Moye LA, Pfeffer MA, et al. A comparison of management patterns after acute myocardial infarction in Canada and the United States. *N Engl J Med* 1993; **328:** 779–84.
5 Pilote L, Califf RM, Sapp S, et al. Regional variation across the United States in the management of acute myocardial infarction. *N Engl J Med* 1995; **333:** 565–72.

Authors' reply

Sir—We thank K S Channer and K M English for their comments. We reported that patients assigned initial strategies of CABG or PTCA had similar risk of death or non-fatal myocardial infarction over a median of 6·5 years of follow-up. We used the phrase "avoidance of myocardial infarction" to indicate that patients had not had myocardial infarction, and did not wish to imply that the risk of myocardial infarction is "reduced or prevented" by either intervention.

We agree that the effects of myocardial revascularisation on the risk of myocardial infarction are not well known, especially in the longer term. We are currently addressing this issue in RITA-2, the largest randomised trial of PTCA versus medical treatment worldwide. Data from 1018 patients followed for an average of 2·7 years show that an initial strategy of PTCA is associated with an increased rate of myocardial infarction, which is mainly attributable to an immediate procedure-related risk.[1] A meta-analysis of the trials of CABG versus medical therapy also reported a high perioperative risk (10·3% death or non-fatal myocardial infarction at 30 days), but after 5 years there was a trend towards a lower risk of death or myocardial infarction in surgically assigned patients.[2]

Since these trials were initiated there have been important advances in surgical and percutaneous coronary interventional techniques, and it is now recognised that lipid-lowering therapy has the potential to improve outcomes for a wide range of patients with coronary artery disease. The effects of contemporary myocardial revascularisation strategies on the risk of myocardial infarction, compared with alternative medical treatment strategies, can therefore only be fully elucidated by further large and properly designed randomised clinical trials.

Robert A Henderson, S J Pocock

*Department of Cardiology, Nottingham City Hospital, Nottingham NG7 2UH, UK; and Medical Statistics Unit, Long School of Hygiene and Tropical Medicine, London

1 RITA-2 trial participants. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. *Lancet* 1997; **350:** 461–68.
2 Yusuf S, Zucker D, Peduzzi P, et al. Effect of coronary artery bypass graft surgery on overall: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994; **344:** 563–70.

Paraquat poisoning

Sir—In their comments on paraquat poisoning in Trinidad, Hubert Daisley and Gerard Hutchinson (Oct 24, p 1394)[1] seem to confuse the issues of unintentional poisoning and suicide. Firstly, there is no evidence that suicide with paraquat is increasing worldwide, indeed, in countries where adequate statistics are available, such as the UK, a substantial decline in the number of cases has been recorded since the early 1980s,[2] despite a steady increase in paraquat use. Secondly, the claim that many unintended deaths occur from paraquat exposure is unsubstantiated. Daisley and Hutchinson do not provide any data, either from Trinidad or anywhere else, to support this claim. In fact, the original work cited in their letter makes no reference to unintentional paraquat poisoning.[3] By contrast, detailed health surveys carried out in developing countries have shown that long-term use of paraquat is safe and does not lead to adverse health effects.[4] Furthermore, formulation and pack changes combined with continuous training and education efforts have led to a significant decrease, if not disappearance, of accidental paraquat poisoning.

The call for prohibition of paraquat is therefore misguided, because it would not address the real issue of suicide in the community, and might

even have the opposite effect of what is intended. Data from Trinidad and Tobago show a 319% increase in male suicide rates between 1978 and 1992, and a significant positive association between suicide and measures of social distress, such as serious crime and unemployment.[5] What would happen to the suicide rate if thousands of subsistence farmers were suddenly deprived of an essential tool that helps them to feed their families and enhance their prosperity? No-one is arguing against limiting the availability of any pesticide, including paraquat, to bona fide users, and efforts to educate farmers about the safe purchase, transport, storage, use, and disposal of pesticides must continue. Let us not be tempted, however, by the suggestion that the complex issue of suicide can be addressed by simple solutions such as banning a product, rather than by concerted, long-term action at the community level. This includes the avoidance of exaggerated statements that may focus public and media attention on any particular agent.

Martin F Wilks

Stewardship Department, Zeneca Agrochemicals, Fernhurst, Haslemere, Surrey GU27 3JE, UK

1 Daisley H, Hutchinson G. Paraquat poisoning. *Lancet* 1998; **352:** 1393–94.
2 Casey P, Vale JA. Deaths from pesticide poisoning in England and Wales: 1945–1989. *Human Exp Toxicol* 1994; **13:** 95–101.
3 Hutchinson G, Daisley H, Simeon D, Shetty M, Lynn D. Paraquat induced suicide in Southern Trinidad. *West Indian Med J* 1998; **47** (suppl 2): 55 (abstr).
4 Howard JK, Sabapathy NN, Whitehead PA. A study of the health of Malaysian plantation workers with particular reference to paraquat spraymen. *Br J Ind Med* 1981; **38:** 110–16.
5 Hutchinson GA, Simeon DT. Suicide in Trinidad and Tobago: associations with measures of social distress. *Int J Soc Psychiatry* 1997; **43:** 269–75.

Authors' reply

Sir—Paraquat, a toxic, non-selective contact herbicide, is used to prohibit the growth of weeds among farm crops. The ecosystem of the fields are also indiscriminately destroyed upon application of this herbicide.

There is nothing misleading about our statement that paraquat poisoning is an issue worldwide and that it is almost synonymous with death. No organ is spared its toxic effects, with the lung being the most severely affected resulting in malignant pulmonary fibrosis.[1] Many treatment protocols have been attempted—haemodyalisis, haemoperfusion, the administration of corticosteroids and immunosuppressants, and even lung transplantation—but they have all been ineffective.

Since its introduction to the Caribbean in the 1970s, paraquat has become established as the main agent of accidental and intentional poisoning. Deaths from self-poisoning in South Trinidad increased from 26 cases in 1972 to 57 cases in 1982. Of the 57 deaths that occurred as a result of poisoning in 1982, 37 (64·91%) people had ingested paraquat, compared with four (15·40%) in 1972.[2] Forensic analysis of acute fatal poisoning in South Trinidad showed that of 105 deaths from poisoning in 1996–97, paraquat was the causative agent in 80 (76·2%) cases.[1]

Yamashita and colleagues[3] reported that of 1000 cases of acute poisoning in a suburb of Tokyo, over 13 years, paraquat was responsible for 291 of the 518 cases of pesticide poisoning, and was most fatal, accounting for 81% of the deaths.

Wesseling and co-workers[4] investigated pesticide poisonings in Costa Rica, with special reference to agricultural workers and occupational exposure, and found that in 1980–86, 3330 people were admitted to hospital and 429 died. Paraquat caused 21% of the occupational accidents, 24% of the hospital admissions and 60% of the deaths. In 1996, 1274 cases of pesticide poisoning were recorded at the poison control centre of Costa Rica; paraquat accounted for 148 cases (11·6%), which is an increase of 48% over the yearly average reported by Wesseling.[4] This report by Leveridge[5] showed that paraquat was responsible for the highest proportion of accidental poisoning among agricultural workers and children aged younger than 9 years.

The reduction of deaths from carbon monoxide poisoning that resulted from the detoxification of domestic gas and from restrictions on its availability, is a testimony to the positive effect on suicide rates of such action.

Although we recognise paraquat's value to the prosperity of subsistence farmers, attention should be directed at decreasing the toxic effects of paraquat in human beings, while maintaining its agricultural efficacy. Emphasis should be placed on the prevention of poisoning from paraquat and the production of an antidote or effective therapy. If these are not forthcoming, then consideration should be given to forbid the use of paraquat in Trinidad.

**H Daisley, G Hutchinson*

Departments of Pathology and Medicine, Faculty of Medical Sciences, University of The West Indies, St Augustine, Trinidad, West Indies

1 Daisley H, Simmonds V. Forensic analaysis of acute fatal poisonings in the southern districts of Trinidad, West Indies. *Vet Human Toxicol* (in press).
2 Rahaman R, Poon-King T. Paraquat as a cause of self-poisoning in South Trinidad (1972–1982). *West Indian Med J* 1984; **32** (suppl): 37–38.
3 Yamashita M, Matsuo H, Ando Y, Tanka J, Yamashita M. Analysis of 1,000 consecutive cases of acute poisoning in the Suburb of Tokyo leading to hospitalization. *Vet Human Toxicol* 1996; **38:** 34–35.
4 Wesseling C, Castillo L, Elinder CG. Pesticide poisoning in Costa Rica. *Scand J Work Envir Health* 1993; **19:** 227–35.
5 Leveridge Y. Pesticide poisoning in Costa Rica during 1996. *Vet Human Toxicol* 1998; **40:** 42–44.

Sir—The ingestion of the herbicide paraquat as a means of committing suicide, which Hubert Daisley and Gerard Hutchinson[1] observed in Trinidad and Tobago, has also been described on a larger scale in Surinam in 1989.[2] The incidence rate of paraquat poisoning in this country reached 211 per million people per year (445 per million in men) and suicide attempts accounted for over three quarters of the detected cases. The dose-related fatality rate was significantly higher in suicidal (74%) than in accidental cases (60%) of paraquat poisoning.

Although we agree with Daisley and Hutchinson that the effect of publishing health and safety guidelines[3] has been limited, we doubt that the communities' awareness on the product's lethal hazard is deficient. The increasing popularity of paraquat as a mode of suicide seems to indicate the contrary.[4] As shown by Perriens and colleagues[2] the incidence of intentional paraquat poisoning is linearly related to its import volume. We do not believe that health education to increase the community's awareness about the product, more strident recognition of its lethal effects, or increased awareness among health professionals about the menace it constitutes, as advocated by Daisley and Hutchinson, will contribute meaningfully towards a reduction in the frequency of paraquat-induced suicide. Limitations on the availability of paraquat to professional users may mitigate the problem, conditional on the successful enforcement of tight regulations, but public-health wisdom calls for a complete ban on its use.

Patrick Van der Stuyft

Epidemiology Unit, Institute of Tropical Medicine, B-2000 Antwerp 1, Belgium

1 Daisley H, Hutchinson G. Paraquat poisoning. *Lancet* 1998; **352:** 1393–94.
2 Perriens J, van der Styft P, Chee H, Benimadho S. The epidemiology of

paraquat (PQ) intoxications in Suriname. *Trop Geogr Med* 1989; **41:** 266–69.
3 Onyon LJ, Volans GN. The epidemiology and prevention of paraquat poisoning. *Human Toxicol* 1987; **6:** 19–27.
4 WHO. Paraquat: health and safety guide. Geneva, Switzerland: WHO, 1991.

Sir—Hubert Daisley and Gerard Hutchinson's letter[1] is important but focuses too narrowly on the problem. Deliberate ingestion of pesticides by impulsive young people is a major problem throughout the tropics. Unfortunately, it is rarely discussed and even less commonly researched in industrialised or developing countries. Concentrating on only one pesticide risks obscuring the more important broader picture.

Paraquat is highly toxic but not uniquely so. Mortality rates have been as high as 80% in Indian case series of aluminium phosphide poisoning.[2] Organophosphate pesticides such as parathion are also highly toxic; although few people die in the well-staffed intensive care units of western hospitals, this is simply not the case in the tropics where case fatality rates of greater than 20% are common. During some months in the rural Anuradhapura district of Sri Lanka, as many as 60% of patients with organophosphate poisoning die, making it the number one cause of hospital death.[3]

Overwhelming pesticide poisoning gives rise to problems rarely seen in the west—Delanty and colleagues' review[4] of medical causes of seizures did not mention pesticides, even though the organochlorine pesticides endosulfan and endrin are the most common cause of status epilepticus in some part of South Asia.[3] A particular concern is that the seizures are usually resistant to conventional therapy and require general anaesthesia, an option not available in most rural hospitals.

Reducing deaths from pesticide poisoning will require multiple approaches, not just "limiting the availability of [paraquat] and providing education". Use of the most toxic pesticides can be restricted but ways must then be found to make the new, safer, and therefore more expensive, pesticides affordable to farmers in the developing world. Education of affected communities is clearly needed to improve the storage of these dangerous substances but, more fundamentally, a long-term approach must be taken to reduce the incidence of self-harm[3] (which often occurs with whatever substance is close at hand, be it medicine, plant seed, or pesticide).

In the mean time, there is a need for clinicians to research pesticide poisoning and, in the absence of specific antidotes, to obtain definitive answers about the efficacy of such non-specific interventions as activated charcoal[5] and pulse methylprednisolone for paraquat. There is no shortage of patients who could be recruited to clinical trials.

**Michael Eddleston, Raveen Pal*

*Centre for Tropical Medicine, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, UK; and School of Clinical Medicine, University of Toronto, Toronto, Ontario, Canada
(e-mail: EddlestonM@aol.com)

1 Daisley H, Hutchinson G. Paraquat poisoning. *Lancet* 1998; **352:** 1393–94.
2 Chugh SN, Dushyat Ram S, Arora B, Malhotra KC. Incidence and outcome of aluminium phosphide poisoning in a hospital study. *Ind J Med Res* 1991; **94:** 232–35.
3 Eddleston M, Sheriff MHR, Hawton K. Deliberate self-harm in Sri Lanka: an overlooked tragedy in the developing world. *BMJ* 1998; **317:** 133–35.
4 Delanty N, Vaughan CJ, French JA. Medical causes of seizures. *Lancet* 1998; **352:** 383–90.
5 Henry JA, Hoffman JR. Continuing controversy on gut decontamination. *Lancet* 1998; **352:** 420–21.

Ageing and cardiovascular disease in developing countries

Sir—In his excellent Nov 7 feature, Larry Husten[1] depicts a realistic world scenario for next decades, and predicts an epidemic of cardiovascular disease in less developed countries. Husten explains the current trend as a result of the increased exposure to cardiovascular risk factors from improvements in economic conditions and increased life expectancy. He also claims that unhealthy lifestyle will, in future, be responsible for cardiovascular disease in developing countries. We do not agree about this statement.

Projections for the period 1950–2050 show that the proportion of the population aged 65 years and older is dramatically increasing in industrialised and less developed countries, as a consequence of the improvements in conditions of life.[2] Furthermore, all main cardiovascular diseases present an age-related incremental trend.[3]

There is no data to discern if the increased exposure to risk factors in less developed countries is mainly due to longer life or to improved social and economical conditions,[4] but we believe that in future longevity, more than lifestyle, will be the main determinant of cardiovascular disease in developing countries. This scenario has already come true in Italy and in other industrialised countries, and the same trend is predictable in developing countries. Our belief accords with the finding that a higher percentage of cardiovascular patients die before age 70 years in less-developed countries, which can be considered a consequence of bad quality medical care, a factor expected to improve in the future.[4]

To predict what will be the future percentage of elderly people among cardiovascular patients is crucial to choose the correct policy. Elderly patients present with different features from middle-aged ones (higher rates of disability and comorbidity and poorer prognosis), and have more serious illness and higher mortality. Congestive heart failure, for example, shows higher incidence and mortality among elderly than among middle-aged people, and requires expensive medical care.

Another issue on which we disagree with Husten is his view that mortality rates in Russia fell in 1984–87 and rose again after this time,[5] as a result of cardiovascular risk-factors (diet, smoking, stress) on cardiovascular disease. Indeed, it is well established that the reduction in life expectancy in Russia and in other eastern European countries is mainly due to other factors during the collapse of the Soviet Union and the subsequent instability, such as high alcohol consumption, bad-quality health services, accidents, and high levels of social violence.[5]

**Gian Luca Iannuzzi, Domenico Acanfora, Giuseppe Furgi MD, Franco Rengo*

*Salvatore Maugeri Foundation, Institute of Care and Scientific Research, Rehabilitation Institute of Telese, Località S Stefano in Lanterria, 82037 Telese T (BN), Italy; and School of Medicine, Federico II University, Naples
(e-mail: cardiotel@fsm.it)

1 Husten L. Global epidemic of cardiovascular disease predicted. *Lancet* 1998; **352:** 1530.
2 Population division of the DFSA. World populations projections to 2150. New York: United Nations, 1998.
3 National Center for Health Statistics. Current estimates from the National Health Interview Survey. Series 10: data from the National Health Survey no 184. Vital and Health Statistics, Hyattsville: National Centre for Health Statistics, 1992.
4 Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation* 1998; **97:** 596–601.
5 Leon DA, Chenet L, Shkolnikov VM, et al. Huge variation in Russian mortality rates 1984–94: artefact, alcohol, or what? *Lancet* 1997; **350:** 383–88.