with optimal local treatments.[12] In some young women with a strong family history of bilateral disease bilateral mastectomy for a small localised breast cancer should be considered and discussed with the patient. Younger women with breast cancer suffer much greater disruption to their lives than older women and have a higher incidence of depression and disease specific intrusive thoughts.

Current evidence suggests that survival of women with breast cancer is improved if they are treated in major centres by multidisciplinary teams. These centres provide the ideal environment for providing support for patients and their families and exploring through clinical trials the most effective adjuvant therapy for individual patients and their cancer.

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1 Nixon AJ, Neuberg D, Hayes DF, Gelman R, Connolly JL, Schnitt S et al. Relationship of patient age to pathological features of the tumor and prognosis of patients with stage I or II breast cancer. *J Clin Oncol* 1994;12:888-94.
2 Early Breast Cancer Trialists' Collaborative Group. Polychemotherapy for early breast cancer: an overview of the randomised trials. *Lancet* 1998;352:930-42.
3 Goldhirsch A, Glick JH, Gelber RD, Senn HJ. Meeting highlights: International consensus panel on the treatment of primary breast cancer. *JNCI* 1998;90:1601-8.
4 Kroman N, Jensen M-B, Wohlhardt J, Mourisden HT, Andersen PK, Melbye M. Factors influencing the effect of age on prognosis in breast cancer: population based study. *BMJ* 2000;320:474-9.
5 Smith TJ, Hillner BE. The efficacy and cost-effectiveness of adjuvant therapy in early breast cancer in premenopausal women. *J Clin Oncol* 1993;11:771-6.
6 Goldhirsch A, Coates AS, Colleoni M, Gelber RD. Radiotherapy and chemotherapy in high risk breast cancer. Letter to the editor. *Lancet* 1998;338:330.
7 Bonadonna G, Zambetti M, Valagussa P. Sequential or alternating doxorubicin and CMF regimens in breast cancer with more than 3 positive nodes: 10 year results. *JAMA* 1995;273:542-7.
8 Henderson IC, Berry D, Demetri G, Cirrincione L, Goldstein S, Martino S, et al. Improved disease-free (DSF) and overall survival (OS) from the addition of sequential paclitaxel (T) but not from the escalation of doxorubicin (A) dose level in the adjuvant chemotherapy of patients (PTS) with node-positive primary breast cancer (BC). *Proc Am Soc Clin Oncol* 1998;17:101a.
9 Early Breast Cancer Trialists' Collaborative Group. Tamoxifen for early breast cancer: an overview of the randomised trials. *Lancet* 1998;351:1451-67.
10 Day R, Ganz BA, Costantino JS, Cronin WN, Wicherhen DL, Fisher B. Health-related quality of life and tamoxifen in breast cancer prevention: a report from the National Surgical Adjuvant Breast and Bowel Project B-1 study. *J Clin Oncol* 1999;70:2659-69.
11 Jakesz R, Gnant M, Hausmaninger H, Samonigg H, Kubista E, Steindorfer P, et al. Combination goserelin and tamoxifen is more effective than CMF in premenopausal patients with hormone-responsive breast cancer study group (ABCSG). *Breast Cancer Research and Treatment* 1999;57:25.
12 Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, et al. Post-operative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy. *N Engl J Med* 1997;337:949-55.

Is CS gas dangerous?

Current evidence suggests not but unanswered questions remain

CS gas (2-chlorobenzylidene malononitrile) is one of the most commonly used tear gases in the world. Law enforcement agencies have found this agent invaluable when faced with combative suspects, for riot control, and for alleviating hostage and siege situations. They use it to help control individuals or groups without the need for lethal force. The chemical was used for crowd control as early as the 1950s, but not until the mid-1960s did it come into common use in several countries. In Britain there has been persistent concern about the use of CS gas in the media, numerous complaints to the Police Complaints Authority, and an editorial two years ago in the *Lancet* that called for a moratorium on the use of CS tear gas.[1] This editorial was unusual in calling for a moratorium on an agent used widely for decades with little data on permanent damage. Nevertheless, it did correctly identify the need for some further studies, as did a report recently commissioned by the British government.[2]

At standard daily temperatures and pressures CS forms a white crystal with a low vapour pressure and poor solubility in water. CS aerosols thus act as a "powdered barb" with microscopic particles which are potent sensory irritants becoming attached primarily to moist mucous membranes and moist skin. The eye is the most sensitive organ in riot control because CS causes epiphora, blepharospasm, a burning sensation, and visual problems. Coughing, increased mucous secretion, severe headaches, dizziness, dyspnoea, tightness of the chest, difficulty breathing, skin reactions, and excessive salivation are common. The onset of symptoms occurs within 20 to 60 seconds, and if the exposed individual is placed in fresh air these findings generally cease in 10 to 30 minutes. In the main the medical literature supports the safety of CS gas.[3–5]

Significant reactions have been reported,[6–8] which may be a result of the way the gas is used. In the heat of a crisis both sides may overreact by excessive use of this agent (the police using too much, rioters throwing canisters back), or the combatants may not leave the area and thus remain exposed and away from the gas's natural antidote—fresh air. In over 30 years of active use of 1% CS gas no lawsuits for damages have been awarded in the litigious environment of the United States. In Britain, however, the spray used by police contains 5% CS in methyl isobutyl ketone (MIBK).

There are no scientific data on the relative safety of 1% versus 5% CS. This is hard data to obtain, since most damage is from aerosol fired at close range, and over half the injuries are "self inflicted" in the sense that the victims voluntarily expose themselves to the gas and remain exposed. Many suspect that the most significant side effects occur in those individuals most active in continuing civil disobedience.

The British Department of Health, with the support of the Home Office, asked three of its advisory committees (on Toxicity, Mutagenicity, and Carcinogenicity of Chemicals in Food; Consumer Products; and the Environment) to study the use of CS spray as a chemical incapacitant because of public health concerns. The report, released last year, stated that many data were available on the toxicity of CS and, to a

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lesser extent, on methyl isobutyl ketone, but only limited data on the formulated product.[2] Based on the data, they concluded that 5% CS in methyl isobutyl ketone did not, in general, raise major health concerns. The committee cautioned, however, that no comprehensive investigations of the effect of CS sprays with follow up in humans are available and they need to be done. They targeted susceptible groups to study in particular: those with asthma or chronic obstructive disease, hypertension, and cardiovascular disease and possibly those taking neuroleptic drugs. The committees also pointed out the need for recommendations for aftercare guidelines for anyone exposed to CS.

This is especially true for ocular exposure. The current recommendations in Britain for treating ocular exposure are to "blow dry air directly onto the eye."[9] The recommendation of the manufacturers of CS in the United States is copious ocular irrigation to dislodge, dilute, and wash away the irritant. The US Army recommends flushing with water or saline and says that impact particles may need to be removed, although no impact CS particles have caused significant ocular damage.[10]

This long-awaited report for the British government will not satisfy many because this issue has marked social and political overlay, and there is incomplete scientific data available to make comprehensive recommendations. Nevertheless, at this point, the committees' recommendations appear reasonable. Based on our current knowledge, if CS tear gas is used by properly trained law enforcement officers and exposed combatants leave the area rapidly, few, if any, significant or long-term human disabling effects should occur.

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1 "Safety" of chemical batons. *Lancet* 1998;352:159.
2 Committees on Toxicity, Mutagenicity, and Carcinogenicity of chemicals in food, Consumer Products, and the Environment. *Statement on 2-chlorobenzylidene malononitrile (CS) and CS spray.* London: Department of Health, 1999. www.doh.gov.uk/pub/docs/doh/csgas.pdf
3 Ballantyne B. Riot control agents. *Med Ann* 1977-8:7-41.
4 Beswick FW. Chemical agents used in riot control and warfare. *Hum Toxicol* 1983;2:247-56.
5 Danto BL. Medical problems and criteria regarding the use of tear gas by police. *Am J Forensic Med Pathol* 1987;8:317-22.
6 Hu H, Fine J, Epstein P, Kelsey K, Reynolds P, Walker B. Tear gas—harassing agent or toxic chemical weapon? *JAMA* 1989;262:660-3.
7 Parneix-Spake A, Theisen A, Roujean JC, Revuz J. Severe cutaneous reactions to self-defense sprays. *Arch Dermatol* 1993;129:913.
8 Ro YS, Lee CW. Tear gas dermatitis: allergic contact sensitization due to CS. *J Dermatol* 1991;30:576-7.
9 Yih JP. CS gas injury to the eye. Blowing dry air on to the eye is preferable to irrigation. *BMJ* 1995;311:276.
10 US Army Medical Research Institute of Chemical Defense. *Medical management of chemical causalties: handbook* Aberdeen Proving Ground, Maryland: US Army, 1995:105-17.

Cholesterol and strokes

Cholesterol lowering is indicated for strokes due to carotid atheroma

Strong correlations between plasma lipoprotein concentrations and the risk of stroke have never been clearly established. Unlike coronary heart disease, there is no significant direct relation between an increased risk of stroke and increased plasma total cholesterol or low density lipoprotein (LDL) cholesterol; nor is there an inverse relation with high density lipoprotein (HDL) cholesterol.[1] Indeed, an inverse relation exists between total cholesterol concentrations and cerebral haemorrhage.[2]

The reasons for this weak or absent relation are several. The most compelling is that virtually all coronary heart disease can be ascribed to coronary atheroma, whereas less than half the incidence of stroke is due to large vessel atheroma. Non-atheromatous causes such as cardiac arrhythmias, small cerebral artery disease, and cortical degeneration are responsible for most of the rest. Another is that, in general, coronary deaths occur at a younger age than strokes, so the population with raised plasma lipids and large vessel atheroma, such as carotid artery disease, is diminished by the age when strokes occur. A third is that plasma total and LDL cholesterol decrease with advanced age, as does their relation to coronary heart disease.[3]

Since no large randomised controlled trial designed specifically to assess the effect of cholesterol lowering in patients with stroke has yet been completed, we need to consider surrogate data from coronary prevention trials and atheroma regression trials (coronary and carotid) in assessing the value of cholesterol lowering.

The evidence of benefit of cholesterol lowering on coronary morbidity and mortality is now incontrovertible. These data come from five large randomised controlled trials of five or more years' duration using a statin to reduce LDL cholesterol in patients with coronary heart disease[4–6] and in asymptomatic middle aged individuals.[7 8] The three largest secondary prevention trials showed that lowering LDL cholesterol concentrations reduced the incidence of coronary heart disease and stroke to a similar degree—but the benefit was for non-fatal strokes.[4–6 9] Even with the large numbers (17 617) of patients with coronary disease included in these trials, it was not possible to conclude that cholesterol lowering reduced stroke mortality. For example, the 4S trial showed that the relative risk of cerebrovascular events was reduced by 37% ($P = 0.024$), similar to the reduction in subsequent coronary events, but the benefit was confined to non-embolic strokes and transient ischaemic attacks. Embolic strokes, haemorrhagic strokes, and those that could not be classified were not reduced.[4] This emphasises that strokes with a basis of large vessel atheroma are most likely to be reduced.

In essence the many coronary atheroma regression trials show that when LDL cholesterol is lowered by at least 20% by a statin or by ileal bypass surgery there is less progression of coronary atheroma and fewer new atheromatous lesions develop. But this improvement is not immediate and may take up to four years of treatment.[10] Statins may, however, have earlier effects on vascular endothelial reactivity and on vasomotor tone—possibly independently of LDL cholesterol lowering—which might be particularly beneficial in stroke patients. Meta-analyses of the coronary preven-

BMJ 2000;320:459–60