L1 . . . may outweigh the risks of its possible toxicity, and its introduction in such patients may now be appropriate" seem overenthusiastic. Certainly it is in stark contrast to an earlier editorial in the *Lancet*, which questioned the efficacy of L1 and drew attention to the unacceptable incidence of side effects, recommending that "this compound should no longer be given to patients."[4]

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1 Kontoghiorghes GJ. Oral iron chelation is here. *BMJ* 1991;**303**: 1279-80. (23 November.)
2 Hoffbrand AV, Bartlett AN, Veys PA, O'Connor NTJ, Kontoghiorghes GJ. Agranulocytosis and thrombocytopenia in patient with Blackfan-Diamond anaemia during oral iron chelator trial. *Lancet* 1989;ii:457.
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4 Oral iron chelators [editorial]. *Lancet* 1989;ii:1016-7.

AUTHOR'S REPLY,—The references cited in my editorial are to my knowledge the major if not the only published reports describing clinical studies with L1. The lack of scientific evidence reported in the editorial in the *Lancet* two years ago[1] did not convince any of the centres to stop testing L1, and now the results of these studies overwhelmingly support the suggestion that L1 is a serious candidate for replacing desferrioxamine. In India, for example, a 35-55% reduction in serum ferritin concentration was observed in 52 patients taking L1 at a dosage of 50-100 mg/kg for one to one and a half years (M B Agarwal *et al*, third international conference on oral chelators in the treatment of thalassaemia and other diseases, Nice, November 1991). L1 has so far been taken daily for six months to two and a half years by 109 out of 230 patients who participated in the trials (papers presented at third international conference on oral chelators in the treatment of thalassaemia and other diseases, Nice, November 1991).[2] Details of these trials will be published in a special issue of the journal *Drugs of Today* next year. The death reported in the editorial may not have been caused by L1.[3,4] Similarly, many patients die while receiving desferrioxamine but the cause of death is not related to this drug.

I agree with N T J O'Connor that the agranulocytosis seen in two patients in the United Kingdom who were receiving L1 at a dosage of 105 mg/kg/day divided into two doses is a serious problem in relation to the development of this drug because of the potentially fatal consequences. The mechanism of this toxicity is not known but may be related to a combination of factors.[5] Weekly monitoring of the white cell count and the use of three or four divided doses each day, which will achieve lower peak serum L1 concentrations, may reduce the incidence of this idiosyncratic toxicity. It should be noted, however, that many other drugs in current use, such as clozapine, penicillamine, and even desferrioxamine in a few cases, have also been reported to cause agranulocytosis.[2,5,6] In the absence of an alternative effective treatment such drugs will continue to be given to patients because of the high benefit to risk ratio. Similarly, chronic transfusional iron overload will progressively cause 100% mortality in the absence of chelation.

As desferrioxamine is not widely used and no other chelator is known to be cheap, orally effective, and relatively non-toxic L1 should be seriously considered as an alternative drug for such patients.

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1 Oral iron chelators [editorial]. *Lancet* 1989;ii:1016-7.
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4 Berdoukas V. Antinuclear antibodies in patients taking L1. *Lancet* 1991;**337**:672.
5 Young GAR, Vincent PC. Drug-induced argranulocytosis. *Clinics in Haematology* 1980;**9**:483-509.
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Coronary heart disease

SIR,—Neither *The Health of the Nation* nor Hugh Tunstall-Pedoe's response[1] addressed one major cardiovascular cause of morbidity and mortality—chronic heart failure—which, in the United Kingdom, is usually caused by coronary artery disease.

The limited epidemiological data available suggest that chronic heart failure is becoming increasingly common and affects up to 500 000 people in the United Kingdom.[2,3] The annual incidence in the older age group is similar to those for myocardial infarction and cerebral infarction,[4] conditions that attracted considerable comment in the secretary of state's document and subsequent responses[1,5,6] (table I).

Furthermore, chronic heart failure causes huge morbidity and mortality (more so than myocardial infarction). It accounts for 5% of all adult medical and geriatric admissions (that is, up to 150 000 admissions a year in the United Kingdom). The annual rate of admission to hospital may approach 45%, with each admission lasting for about eight days. The economic implications are obvious.

Many admissions in patients with chronic heart failure might be preventable. Angiotensin enzyme inhibitors reduce the need for admission for worsening heart failure. The annual rate of admission in the studies of left ventricular dysfunction (SOLVD) was about 2% for patients with thromboembolic events and about 4% for those with pulmonary infection.[7] Anticoagulation and vaccination (pneumococcal/influenza) might help reduce these admissions (these might be areas for future study).

The dreadful mortality due to chronic heart failure also deserves mention. Recent studies have confirmed the dismal prognosis reported in the Framingham study, in which half of patients died within five years of diagnosis despite conventional treatment with diuretics and digoxin (mortality worse than that for stage II breast cancer and similar to that for stage II squamous cell carcinoma of the lung).[7,9] These studies have also, however, shown that treatment with angiotensin converting enzyme inhibitors can reduce mortality in chronic heart failure—by 30% at one year in severe chronic heart failure and by 16% at four years in mild to moderate chronic heart failure.[7,9] Angiotensin converting enzyme inhibitors have been shown to be easy to use and relatively free of adverse effects in these patients.[7,9] Furthermore, they are very cost effective (table II).

Chronic heart failure is therefore a major public health problem that has been neglected in the United Kingdom. As few as one fifth of patients with chronic heart failure in the United Kingdom are treated with an angiotensin converting enzyme inhibitor. More effort must be made to ensure that chronic heart failure is recognised and treated. Issues such as the earlier detection and prevention of progression of left ventricular dysfunction need to be discussed, particularly in the light of the positive findings in the prevention arm of the studies of left ventricular dysfunction.

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TABLE I—*Age adjusted annual incidence of myocardial infarction, cerebral infarction, and chronic heart failure/1000 at 30 year follow up in Framingham study*[6]

	Myocardial infarction		Cerebral infarction		Chronic heart failure	
Age (years)	Men	Women	Men	Women	Men	Women
35-64	6	2	1	1	3	2
65-94	13	7	5	4	10	8

TABLE II—*Cost effectiveness of treatments*

Treatment	Problems prevented per 1000 years of treatment or *per 1000 patients treated
Treatment of mild hypertension	1-2 strokes
Lipid lowering treatment (gemfibrozil)	2-3 cardiac events
Intravenous β blockade after myocardial infarction	6 deaths*
Oral β blockade after myocardial infarction	17 deaths
Intravenous streptokinase after myocardial infarction	25 deaths*
Enalapril for severe chronic heart failure	160 deaths
Enalapril for mild or moderate chronic heart failure	16 deaths 116 admissions

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9 Cohn JN, Johnson G, Ziesche S, Cobb F, Francis G, Tristani F, *et al*. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. *N Engl J Med* 1991;**325**:303-10.

AUTHOR'S REPLY,—*The Health of the Nation* did not set out to target all major causes of mortality and morbidity. The key areas chosen had to be major causes of premature death or avoidable ill health; areas where effective interventions are possible; and, thirdly, and most relevant to J McMurray and H J Dargie's argument, "ones in which it is possible to set objectives and targets and monitor progress towards achievement through indicators."[1] McMurray and Dargie make an impassioned plea for recognition of chronic heart failure but admit that the bulk of the problem occurs in those over the age of 65. The uphill task that they have in getting chronic heart failure recognised as a key area is shown by the routine mortality statistics for England and Wales (table), in which it seems to account for only one death in 1000 below age 65.[2]

Heart failure shares the fate of other conditions such as hypertension, hypercholesterolaemia, cigarette smoking, and ventricular fibrillation, which contribute either as risk factors or as pathological mechanisms. They are likely to be left off the death certificate and, if they do appear, will be coded as the cause of death only if no specific underlying cause is coded with them. Such factors or processes cannot be studied from routine