to chloroquine fair protection will probably be obtained from a regular weekly dosage of 300 mg of chloroquine base during the stay in the endemic area and for at least four weeks after return to a temperate climate.¹⁸ Should a breakthrough occur other antimalarials will have to be used for treatment, including mefloquine when it becomes more widely available.¹⁵

Primaquine, normally used for preventing relapses in *P vivax* malaria, should be avoided or used with great caution in any pregnant woman with a risk of deficiency of glucose-6-phosphate dehydrogenase. There is no evidence that chloroquine chemoprophylaxis causes any toxic effects on the eye or any congenital defects when given at the standard adult dosage of 300 mg base a week for as long as four to five years.¹⁷ Adverse effects of chloroquine on the auditory system of the newborn were reported when the drug was given in very high dosage to pregnant women with rheumatoid arthritis and similar diseases. No such effects have been reported from malaria prophylaxis.

Like most of the other antimalarial drugs chloroquine crosses the placenta and appears in small amounts in maternal milk,¹⁰ but this does not provide a full safeguard for the newborn baby, and the time honoured methods of protection from mosquito bites (bed nets, space sprays, and so on) need to be used.³

Finally, a traditional and usually unwelcome piece of advice given to any woman in her second half of pregnancy is to forgo any exotic travels unless unavoidable.

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A cooler look at lead

"The things we would like to know may be unknowable, so there is some virtue in just getting rid of the problem," said Sir James Gowans, commenting on the issue of lead and intelligence at the end of a conference on lead held in Cardiff last week. Organised by the Medical Research Council Epidemiology Unit and the area postgraduate organiser, this meeting came in the wake of the Royal Commission on Environmental Pollution's report recommending the removal of lead from petrol.¹ Now that the Government's decision on petrol has put an end to this long and bitter controversy, a cooler look can be taken both at the scientific questions and at the other practical actions that are needed.

The royal commission reached its conclusion on grounds of prudence, without making any judgment about the evidence on the effects of low concentrations of lead on children's intelligence and behaviour. It was particularly worried that such a persistent and widely distributed toxin as lead should have so narrow a safety margin, but its conclusions were "not dependent on the precise accuracy of any particular investigation or calculation." This approach is welcomed by the *BMJ*, which has for some time urged the abolition of lead from petrol while remaining agnostic about some of the scientific evidence.²

Nevertheless, the effects of low concentrations of lead on children are still relevant to the urgency and the extent of the various practical actions recommended by the royal commission. In the last session of the Cardiff conference Marjorie Smith reviewed the evidence, including the Institute of Child Health and Southampton University study with which she was concerned and two others reported recently at the British Psychological Society's annual conference in York. The first of these three studies, on tooth lead in 6-7 year old London children, is the most extensive and detailed yet carried out. On the IQ scales and the reading test there were significant differences between the "high," "medium," and "low lead" groups; but after social variables were allowed for the differences became non-significant. The other two recent studies similarly showed differences in performance favouring children with the lower lead burdens but these too turned out to be non-significant.

What are we to make of these findings, taken in conjunction with the more positive earlier reports (reviewed in a recently published symposium³)? All the trends are in the same direction, and Marjorie Smith did not believe that they could be attributed to chance. Nevertheless, since controlling for all social variables was impossible the differences could well have resulted from social factors rather than differences in body burdens of lead—and if there was in truth a "signal" due to lead, she concluded, it might be undetectable amidst the "noise" of other factors. Rutter has presented arguments for accepting that the trends do represent a genuine though small effect of lead; and he makes two further important points—that an average reduction in IQ of only a few points in any group of children implies more damaging impairment in some of them, and that a given dose of lead may possibly do more harm to the socially disadvantaged children.³

Wherever the truth lies, there is a strong enough possibility of risk to justify energetic measures against lead exposure of all kinds. Lead in water still needs action.¹ Replacement of lead pipes gives a dramatic fall in both water and blood lead concentrations^{4 5} but it costs some £600 a house and the work proceeds slowly. But for once the cheap solution begins to look like the superior one, and P C Elwood discussed the arguments

for hardening the water supply instead (which would also protect against lead solder in modern plumbing). At any concentration of water lead hard water is associated with blood lead concentrations only 60% of those found where the water is soft.⁶ Calcium and phosphate interfere with the absorption of lead, including probably lead from other sources, notably food⁷; and this would explain the MRC Epidemiology Unit's interesting findings that hardening the water supply with calcium salts lowers blood lead concentrations more than would be expected from the fall in water lead, and even reduces blood lead in areas with a negligible amount of lead in the water. These conclusions are preliminary and research is still in progress; but as hardening water should also reduce cardiovascular disease the idea looks doubly promising.

The importance of attending to all sources of lead and not just petrol is shown by the epidemiology unit's blood lead surveys, discussed at the conference and to be published in the *BMJ*⁸ (see letter on p 1515). The data show a fall in blood lead concentrations during the last decade or so in the Welsh people surveyed of from 23% to 40%—in the absence of changes in traffic or in the water supplies. Diet (including less lead from canned food) is the most likely source of the improvement, though other factors may have played a part.

Some of the highest blood lead concentrations can be traced to leaded paint ingested by young children, and several of the royal commission's recommendations concern paint, though this was not discussed at the Cardiff conference. Local authorities should have access, says the report, to modern equipment for detecting lead in paintwork in situ. In the United States a hand held x ray fluorescence instrument, the XK-3 Lead-in-Paint Analyzer (Gamma-Tech, Princeton), has been available for some time, enabling the lead content of a painted surface to be obtained in seconds without marring the paintwork. It has not yet been acquired here. The initial cost of the instrument should be set against the simplicity of the operation and the possibility of large scale and effective surveys. At the same time, as the commission says, there should be more publicity about the dangers of old paintwork. Dust and also soil can be important sources of lead in young children⁵ and more attention should be given to these too, especially in areas of industrial pollution.

Finally, the setting of a timetable for phasing out lead in petrol must not let the Government, local authorities, or anyone else lose sight of the urgency of other action, including monitoring of lead levels and reducing exposure from whatever source and on however local a scale. It might make a lot of difference to some, perhaps many, children in the next few years.

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Staff editor, *BMJ*

Hyperthyroidism and the heart

Thyroid hormones have positive chronotropic and inotropic effects on the heart, with the result that in hyperthyroidism cardiac rate and cardiac output rise. The maximum velocity of fibre shortening¹ and myocardial excitability² increases, the circulating blood volume expands,³ and the pulse pressure widens.⁴ The patient complains of palpitations and intolerance of exertion and is at risk of the complications of tachyarrhythmias, such as thromboembolism and cardiac failure.⁵ These events are no longer thought to be due to increased circulating concentrations of catecholamines or to an increase in sensitivity of the heart to catecholamines induced by thyroxine.⁶⁻⁹ The most favoured explanation is that in patients with hyperthyroidism the heart has an increased density of adrenoceptors.¹⁰

Nowadays cardiac performance can be assessed by relatively simple and non-invasive measures such as systolic time intervals (derived from simultaneous tracings of the electrocardiogram, phonocardiogram, and carotid pulse)¹¹ and left ventricular ejection fractions,¹² which correlate well with the rate of rise of ventricular pressure (contractility) and the stroke volume. Many studies have shown that myocardial contractility is increased in hyperthyroid patients at rest,¹³⁻¹⁵ but its response to exercise has not been investigated.

Myocardial contractility and heart rate normally increase with exercise, but a recent report from Edinburgh suggests that in hyperthyroidism the contractile performance of the heart falls during exercise, despite an increase in heart rate.¹⁶ This paradoxical response returns to normal when the patient becomes euthyroid. Furthermore, propranolol reduces exercise induced tachycardia in both groups, and will attenuate the rise in contractility in normal, but not the fall in hyperthyroid patients. The response of heart rate to exercise during beta-blockade was reported some time ago in hyperthyroid patients,¹⁷ but the Edinburgh study¹⁶ is the first to investigate ventricular contractility under such conditions. It appears that the exercise induced rise in heart rate in hyperthyroidism is mediated by beta-adrenoceptors, though the fall in myocardial efficiency which accompanies it is not. The authors conclude that the reduced contractility on exercise in hyperthyroidism results from a form of reversible cardiomyopathy, perhaps the direct effect of exposure to excess amounts of thyroid hormones.

What are the clinical implications for the heart in hyperthyroidism? Seemingly the only satisfactory way of restoring myocardial function, even in uncomplicated hyperthyroidism, is to restore the raised serum hormone concentrations to normal as quickly as possible, with antithyroid drugs, surgery, or radioiodine as appropriate to the patient's age, size of goitre, and cardiac state.¹⁸ Treatment with beta-blockers alone is not satisfactory long term: they seldom provide complete control of symptoms,^{19 20} have a low remission rate,^{20 21} and—according to the Edinburgh experience¹⁶—fail to influence myocardial contractility. The Edinburgh findings may explain why hyperthyroid patients often show impaired exercise tolerance, though the improvement in dyspnoea on effort reported in patients treated with propranolol alone requires clarification.¹⁹

Cardiac failure is uncommon in hyperthyroidism, but 10-15% of patients have atrial fibrillation,²² and 60% of these will revert spontaneously to sinus rhythm when treated for the hyperthyroidism.²³ Accordingly, a diagnosis of "lone atrial

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