the "readiness to change" of practices that were prepared to invest in good management.

Although the labour party proposes to replace fundholding with locality commissioning, in reality none of the political parties seem likely at present to abolish the fundholding scheme. Indeed, while the Audit Commission was undertaking its research, the scheme was expanded to include total fundholding and community fundholding. However, the commission's report makes depressing reading for those who would like to believe that fundholding is the answer to the NHS's problems. Policies, like clinical interventions, should be fully evaluated before being implemented, if public monies are to be used to greatest effect. The current priority for the NHS and the research community must be to address the question of how to transform the fundholding scheme so that it enhances the NHS's capacity to improve the public health. This question needs answering urgently, before the NHS is subjected to yet another unevaluated change of policy.

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Chronic neurological effects of organophosphate pesticides

Subclinical damage does occur, but longer follow up studies are needed

Organophosphate pesticides have replaced organochlorines in the past 20 years and are widely used in both agricultural and structural applications. People working with these compounds receive the highest exposures, but the public can be exposed during structural applications or by drift from aerial spraying. The immediate toxic effects of organophosphates are well described; what remain controversial are the longer term effects.

Organophosphates inhibit the neurotransmitter acetyl cholinesterase, leading to symptoms related to the autonomous nervous system (abdominal cramps, nausea, diarrhoea, salivation, miosis) and the central nervous system (dizziness, tremor, anxiety, confusion). Symptoms usually occur within hours of exposure and typically disappear within days or weeks as new cholinesterase is synthesised. The degree (or rate) of inhibition required to produce symptoms is controversial.

On the basis primarily of animal data and human case reports we know that some organophosphates (such as methamidophos, leptophos, fenthion, merphos) inhibit a second enzyme, neuropathy target esterase. Severe inhibition of this enzyme (animal data suggest inhibition by 70% or more) may be accompanied by a peripheral neuropathy 10-14 days after exposure. This delayed neuropathy typically affects the motor and sensory nerves of the legs and is caused by a "dying back" of the distal axons. Symptoms include tingling sensations with weakness and ataxia that develop into paralysis in severe cases. Effects are often reversible but may persist. A famous human epidemic of delayed neuropathy induced by organophosphate occurred in the United States in 1930 after ingestion of a headache remedy (Ginger Jake) contaminated with triorthocresyl phosphate. Over 4800 cases of delayed neuropathy were reported, often with persistent severe effects.[1]

Epidemiological studies are sparse but suggest that exposure to organophosphate pesticides can induce other chronic effects on the central and peripheral nervous system, either after acute intoxication or as a result of lower level long term exposure.[2]

Acute intoxication with organophosphates remains a problem in industrialised countries; an estimated 3000-5000 cases of accidental systemic poisoning by organophosphates occur annually in the United States (J Blondell, Environmental Protection Agency, personal communication). In the developing world an estimated three million severe pesticide poisonings occur annually, of which 220 000 are fatal. About 3% of the agricultural workforce in developing countries is estimated to suffer some symptoms each year.[3]

Three large epidemiological studies have examined the chronic effects among patients poisoned by organophosphates. Savage *et al* studied 100 patients admitted to hospital and matched controls an average of nine years after poisoning.[4] They found significant deficits among the cases on several cognitive tests of memory and abstraction but no differences on electroencephalography or neurological examination. No analyses for specific pesticides were done. Cases had worse reading ability than controls, and educational differences may have accounted for the results. Rosenstock *et al*[5] and McConnell *et al*[6] studied 36 men poisoned by organophosphates (mostly methamidaphos) who had been admitted two years earlier, as well as matched controls. They found several cognitive deficits in the poisoned subjects and a significant decrease in vibrotactile sensitivity, an indicator of peripheral neuropathy. Finally, Steenland *et al* studied 128 men poisoned a mean of seven years earlier and 90 controls. Vibrotactile sensitivity and one cognitive test (sustained attention) were significantly worse in the poisoned men, and several tests showed deficits which increased with the severity of the poisoning. Nerve conduction tests and clinical neurological examination showed no differences.

Studies of subjects with long term lower level exposure are also suggestive but not as consistent as studies of poisoned subjects. For example, Ames *et al* studied 45 professional pesticide applicators using a variety of organophosphates who had had at least one documented episode of cholinesterase inhibition but no symptoms.[8] In comparison to 90 controls, no central or peripheral nervous system effects were observed. On the other hand, Stokes *et al* studied 68 long term (mean of 20 years) pesticide applicators and 68 matched controls, tested during the off season.[9] The principal organophosphates used were guthion, chlorpyrifos, and diazinon. The applicators showed a significant decrease in vibrotactile sensitivity. Stephens *et al* studied 146 sheep dippers and 143 controls months after exposure.[10] These men averaged 15 years of sheep dipping, and the principal organophosphates were diazinon, propetamphos, and chlorfenvinphos. The authors found significant exposure effects on neurobehavioural tests that examined sustained attention and speed of information processing but no effects on memory or learning.

In summary, therefore, well designed studies have shown chronic subclinical damage to the central and peripheral nervous system among those previously poisoned by organophosphates. Studies of subjects with long term low level exposures have been less consistent, but some have also shown subclinical effects on the central and peripheral nervous system. Low response rates and possible selection biases have affected

almost all studies but are unlikely to explain the observed effects; indeed loss to follow up of more severely affected individuals may have caused some bias towards showing no effect. Differences between studies may be due to the different organophosphates studied. The observed peripheral effects are consistent with persistent delayed neuropathy induced by organophosphate. The mechanism by which chronic central nervous system effects might occur is unknown; Duffy *et al* have observed persistent changes on electroencephalograms after high level exposure.[11]

Clinical neurological examinations have given negative results in the subjects studied epidemiologically. The importance of the observed subclinical effects on quality of life or day to day functioning may be minimal. The study subjects generally were not followed for long periods, and we do not know whether the observed subclinical effects will diminish, persist, or get worse. This question is important in the light of the large number of people exposed and in the light of some case reports which suggest that more severe long term effects are possible.

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Bovine spongiform encephalopathy: its wider meaning for population health

Worldwide intensive meat production is unsustainable

Evidence from Britain that the agent causing bovine spongiform encephalopathy in cattle may cause neurological disease in beef eaters[1] and the consequent turmoil in the beef trade have made compelling headline news across Europe. The ecological dimensions to this public drama have, however, even wider implications for population health.

Three issues warrant discussion. Firstly, although the infective agent of bovine spongiform encephalopathy and its effects may seem exotic, this episode merely extends the long running narrative whereby changes in human culture induce new infectious diseases. Secondly, the method of cattle feeding implicated in the transmission of bovine spongiform encephalopathy seems partly to have arisen because of supply-demand pressures in the world food production system. Thirdly, the scare about bovine spongiform encephalopathy is the tip of a much larger iceberg of adverse environmental and health consequences of the mass production and consumption of meat.

Firstly, incredulity that the mysterious transmissible agent responsible for bovine spongiform encephalopathy might "jump species" and infect humans is misplaced. Microbes and their ilk are no less opportunistic than any other species—and are capable of rapid genetic adaptation.[2] We humans have improved our survival prospects by widening the range of other species on which we feed. Bacteria and multicellular parasites do likewise, as do the viruses and prions that parasitise the intracellular molecular processes of animals and plants. Ever since humans made intimate contact with other animal species—by intruding on their habitats, eating them, or domesticating them—mutant strains of zoonotic agents have opportunistically become infectious agents in humans.[3 4] Thus have we acquired smallpox from cattle, measles from ungulates or dogs, influenza from pigs, HIV from monkeys, and so on.

This endless narrative is a condition of life on earth: it is simply anthropocentrism that sees many tiny species as "pests and diseases" because they share our food supplies or parasitise us. Modern intensive methods of agriculture, animal husbandry, and aquaculture have opened up vast new ecological opportunities for microbes.[4 5] Hence it would be surprising if transmission of the type that we think may be happening with bovine spongiform encephalopathy and Creutzfeldt-Jakob disease did not occur.[6] Recent sequencing of the prion protein in vertebrates indicates an evolutionary connection between the forms in cattle and in humans.[7]

Secondly, modern methods of intensive farming reflect increasingly the tension between food supply and demand. As populations have increased in size and affluence, so the demand for food has grown, particularly for foods such as meat that are seen as high quality. The expectation of cheap meat, helped by competition between supermarkets and government subsidy, is spreading throughout the world's middle classes. The resulting intensification in meat production requires heightened inputs of energy, chemicals, water, and protein feed.[8]

The use of protein derived from ruminants for cattle feed increased in the early 1980s, as world prices escalated for the then prevailing protein supplements, fishmeal and soybeans. The price rises reflected faltering growth in per capita production of those foods, after three decades of strong growth.[9 10] The per capita production of soybeans tripled between 1950 and 1980 while the per capita fish catch doubled between 1950 and 1970, but neither has increased further since those peaks. From the 1980s the growth in production of these and several other foods seems to have fallen behind the growth in world population.[10 11] We must therefore ask of our recent methods of food production: to what extent have we been depending on unsustainable resource inputs? And of the future: can we sufficiently boost production with genetically engineered plant, animal, and marine foods? The answers bear strongly on the long term prospects for human health.

Thirdly, beef production is a very environmentally damaging form of meat production.[8] If we are adequately and equitably to feed a world of 10 billion people next century, compared with today's 5.7 billion, then beef-eating Westerners