model of agent, host, and environment.²⁸ Research that allows for interplay among these factors is likely to be most productive.²⁹ We already know much about the environments in which multiple sclerosis is common and about relevant host factors (including those with a genetic basis). The agent(s) remains a mystery, although an infectious agent has long been suspected. More than 20 viruses have been linked with multiple sclerosis over the years, but in no case has the association proved causal.³⁰ Recent reports implicating a retrovirus have not been confirmed.³¹⁻³³ Alter *et al* suggested that multiple sclerosis might be an age dependent host response to measles and other childhood infections.^{34 35}

Another lesson from the history of epidemiology is that diseases may be preventable before their causes are properly understood. Thus the Royal Navy knew how to prevent scurvy more than a century before the discovery of vitamins, and John Snow's work led to steps to control cholera long before the cholera vibrio was identified.²⁸ Some optimists hope that the vaccination programmes against measles will lead to a decline in multiple sclerosis. That remains to be seen, but the search for environmental factors should continue.

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Picking up the tab for erythropoietin

General practitioners should prescribe it—just as they prescribe growth hormone

One of the satisfactions of renal medicine is that chronic dialysis works. This treatment has kept some patients alive for more than 20 years. Nevertheless, survival is not cheap for government or patient. Maintenance haemodialysis or continuous ambulatory peritoneal dialysis costs £10 000-£12 000 a year, and about 8000 patients receive such treatment each year in the United Kingdom. Only recently has the struggle for sufficient dialysis facilities ended: the memory of "negative selection"—patients left to die of chronic renal failure—is still fresh.^{1 2} About a quarter of patients receiving dialysis still feel unwell because of anaemia caused by erythropoietin deficiency. Treatment with erythropoietin is available, but it is very expensive. A year's treatment for one patient costs £3000-£5000. Now a new battle is enjoined.

Taylor and colleagues have presented their findings in a group of patients receiving dialysis before, during, and after an eight week course of maintenance erythropoietin (p 272).³ The hormone was provided for trial purposes by the manufacturers. Because funds were not available to purchase further supplies, treatment had to be stopped. In all 12 patients the wretched symptoms of erythropoietin deficiency anaemia recurred, with an appreciable psychological morbidity.

Regrettably these are not isolated observations; many British renal units experience similar difficulties. It is not easy to estimate how many patients have the difficulties described by Taylor *et al*. The suppliers estimate that about 1300 patients have been treated with free erythropoietin made available for clinical trials and believe that most patients continue to enjoy the benefits of the hormone purchased from renal budgets. Yet their estimate is difficult to reconcile with Taylor *et al*'s paper and what one hears on the grapevine. Certainly not all those who need erythropoietin are receiving it; perhaps 200-300 patients are missing out. Renal budgets that are underfunded (and hence overspent) are to blame. The treatment is successful,^{4 5} and the lack of funds to purchase supplies is scandalous. Money from a general hospital budget spent on erythropoietin would reduce the available acute sector funds even further. The Department of Health has, however, made it clear that central funding will not be provided for this desirable hormone.

Faced with these difficulties, what should doctors do? Blood transfusions, though ameliorating symptoms for a few weeks, are not the answer. Supplies are short, repeated transfusion leads to iron overload, and most important is the

real risk of sensitisation of patients receiving dialysis to human leucocyte antigens, which may make matching for a transplant difficult or impossible. A successfully transplanted kidney produces erythropoietin such that the anaemia of chronic renal failure is corrected by three to four months after transplantation. Unfortunately, the number of patients waiting for a graft kidney is increasing year by year. Perhaps two fifths of all dialysis patients are too old or too infirm to hazard the risk of transplant surgery and immunosuppression.

An obvious way forward when the renal budget is too small is to ask the patient's general practitioner to prescribe the hormone. This arrangement exists for growth hormone. The Secretary of State for Health has specifically directed that growth hormone, which costs £5000-£10 000 a year (supplier's estimate) should be prescribed by family doctors. Many general practitioners are prescribing erythropoietin, but not all are happy to do so.

Some think that it is improper to prescribe drugs for patients whose treatments are not directly under their clinical control,⁶ and they cite the Department of Health's backing for this position. It has issued reminders to practitioners that prescribers should be in clinical control of all patients for whom they prescribe. Presumably this is yet another attempt

to restrict funding without consideration for patients' welfare and contradicts previous statements from the Department of Health that all who require a drug will receive it.

The way around this difficulty? Reluctant general practitioners should be asked to take full responsibility for their patients' welfare and renal physicians should provide just advice when the patient is not in hospital. The time and effort that this would take for a few hundred patients would be well worth while. Erythropoietin so improves the quality of life in selected patients that to withhold it, in 1991, in the United Kingdom is unacceptable.

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Prospective or retrospective: What's in a name?

The shorthand classification of a study may create confusion

The recent adoption of the more informative structured abstract by several medical journals has rehashed an old debate on the use of the words "prospective" and "retrospective" in clinical and epidemiological research.¹ The structured abstract requires a description of the study design. Editors like it to be crisp and clear and, above all, short. Hence the words prospective and retrospective have started a second life—and seeded new confusion.

Epidemiology knows of two schools of thought regarding the use of these words. One school, originally centred on epidemiologists at Johns Hopkins, calls any follow up study prospective even if it is clearly a historical cohort,^{2,3} maintaining that any follow up moves forward in time. They therefore use the word retrospective for what the other school calls "case-control." Their reasoning is that in the case-control study the investigator in effect looks back from present disease to past exposure. The other school, originally centred on Harvard,⁴ knows of two types of follow up studies—the prospective and the retrospective—both distinct from case-control research. According to the second tradition, the strictest definition of a prospective study might run thus: a follow up study in which a disease outcome is related to baseline characteristics that were originally collected with this particular follow up in mind. The investigators collected the baseline information according to a protocol that included the follow up and then aged together with their subjects. In contrast, in a retrospective follow up study the investigator has a bright idea, searches some conveniently available data—originally collected for other purposes—and adds a follow up about his or her favourite disease up to the present. The second school maintains that it sticks to the common use of the prefixes "retro" and "pro," as indicators of the time course of a study from the point of view of the investigator.⁴

In the past feelings ran high, and present positions remain entrenched. The *Dictionary of Epidemiology* still calls "cohort," "follow up," and "prospective" synonyms, irrespective of

whether the data are past or present,⁵ while clinical epidemiologists and theoreticians detail all the distinctions.^{6,7} Smart researchers have, of course, learnt that the chances of funding and publication are improved by calling a study prospective. The qualifier retrospective has been defamed too often in the past, accused of all the potential biases of case-control research.⁸

In the *BMJ*'s recent clinical and epidemiological papers adorned with the new type of abstract the word prospective abounds. A closer look at the details of the methods in these papers, however, soon shows that the use of the word wildly transgresses the boundaries of the venerable epidemiological conflict of terminologies. Several case series are called prospective, apparently because the patients were entered consecutively, even when there is no inkling of any prespecified research plan: data were retrieved from more or less consecutive old records because of a new interest. Oddly enough, plain case-control comparisons within such patient series also happen to be labelled prospective, presumably because the patients accrued over a specified period. Almost all follow up studies, whether of past or present cohorts, wave prospective flags. Some are prospective according to the strictest definition. In others researchers who retrieved an old population survey, a previous case series, or a forgotten clinical trial and who added a further follow up for a purpose unrelated to the original venture proceed to call the amalgam prospective. Furthermore, when data from a follow up study of whatever sort are reanalysed for a new purpose the new publication almost invariably retains the label prospective; the proper name should, of course, be "secondary analysis." Finally, a common superfluous use of the word is in the expression "prospective randomised controlled trial." As people cannot be randomised in the past a randomised controlled trial cannot be anything but prospective. Given the confusion—which is not limited to this journal—the words prospective and retrospective have lost all meaning. From spotting them