that rather intangible quality ‘clinical judgment’ nor rigorous laboratory analyses will enable us at present to identify the specific individuals within a larger treated group who will benefit from a particular treatment. This is not to say that ignorance will always remain at this level. Molecular genetics carries the promise of defining the heterogeneity of disease much more closely. This has already occurred in rarer forms of diabetes and hypertension and inevitably the process will continue as a natural development of previous decades of scientific and clinical research which have identified hypertensive and diabetic individuals as high risk groups in the general population. Laboratory science is from this perspective a further natural development in disease characterization.

This example helps us to recognize one form of uncertainty which remains despite major scientific advances; that is, the uncertainty attributable to persisting shortcomings in our understanding of disease. This is unlikely to be wholly resolved but the evolution of knowledge will help us to define risk and therefore treatment and potential benefit much more precisely, so that perhaps only three children with otitis media rather seven, or five rather than ten hypertensive patients require treatment. It will be observed when Professor Klein’s example is taken further in this way that judgment by the clinician confronting the individual case assumes even greater importance in the assimilation of a complex system of clinical and laboratory evidence.

The other example cited by Professor Klein underlines a second form of uncertainty confronting society and its surrogates in decision-making. There is, we are told, a division of opinion between health authorities on whether to fund in vitro fertilization. There is excellent scientific evidence in favour of the effectiveness of this procedure; the source of debate is whether IVF is a justified call upon NHS funds. Research data could still of course illuminate this decision—for instance, by identifying more closely the factors which lead to success and therefore limit wastage of resources upon ‘failures’. Nevertheless, this clearly could not resolve a debate which entails a judgment about what is appropriate for the NHS to provide. The same argument could be applied to all forms of NHS activity. The final decision about whether to carry out a procedure or not is a judgment of value. This should be informed by scientific evidence but cannot be made by the inductive method alone. I have elsewhere used the example of hypertension treatment to illustrate the sophisticated nature of this judgment in the face of a demonstrable spectrum of benefit, which extends at one extreme from net financial returns to society as a result of treating high-risk individuals to an opposite extreme where mass treatment of the mildest forms of hypertension produces individual benefit at exorbitant cost to society. Within this range, a judgment has to be made which ultimately reflects society’s values. Scientific research can illuminate but cannot make such a decision. An ‘ought’ cannot be derived from an ‘is’.

It is no coincidence, perhaps, that the issue of the QJM which concluded with Professor Klein’s article began with a plea for more relevant clinical trial evidence on the indications for beta interferon treatment of multiple sclerosis in the face of massive cost to the NHS. But even when such major scientific uncertainties are resolved, society is still confronted with fundamental questions of value in deciding what is a worthwhile investment. Science clarifies but does not resolve the debate. Professor Klein clearly accepts this but then obscures fundamental issues with an irrelevant attack upon the myth of ‘scientism’.

J.D. Swales

Director of Research & Development
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References


Sirs,

I am delighted to have drawn fire from Professor Swales, since this allows me to clarify my argument. I obviously failed to make myself clear in one crucial respect. In exploring the limits of the new scientism (a term about which I remain unapologetic) it is important to distinguish between: (i) the contribution of scientific knowledge to the way in which the medical profession collectively and individual clinicians define ‘good practice’; (ii) the use of scientific knowledge in policy-making and purchasing, in the NHS.

My reservations about the new scientism focus entirely on (ii). The purpose of my paper was to draw attention to the limited scope for using scientific evidence to shape purchasing and to control medical
practice. So, for example, the Management Executive is pushing hard for health authorities to ‘disinvest’ in procedures or forms of treatment where evidence about effectiveness is lacking, and to switch funds to those services where there is evidence that they will produce health gains. But this is to ignore that ‘effectiveness’ is a conceptually slippery notion, particularly when applied to heterogeneous groups. Similarly, the notion of ‘health gains’ remains elusive: there are good reasons for scepticism about the various attempts that have been made to translate it into techniques for calculating the benefits yielded by different treatments in order to prioritize between competing claims on resources.

I therefore come to the same conclusion as Professor Swales: indeed his arguments seem to reinforce rather than contradict my thesis. This is that scientific knowledge can illuminate but cannot resolve the dilemmas of choice in the NHS. Where I differ from him is in taking the rhetorical aspirations of the Department of Health more seriously than he does. Hence my conclusion: if the scientific community feeds these aspirations, sooner or later there will be a backlash.

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References


Imipramine and amitriptyline in hyperactive children

Sir,

There seems to be almost a campaign in the media about the use of Ritalin (methylphenidate) in the treatment of hyperactive children. Anyone who has lived, for even a short time, with such a child has sympathy with the parents, especially when it is said there is no alternative to Ritalin. If people were told of the close chemical relation between Ritalin and ‘Ecstasy’, they might not be so keen on the former. It is unfortunate that the use of tricyclic antidepressants is rarely mentioned.

Comparative studies between imipramine or amitriptyline and methylphenidate have been described and a double-blind cross-over study with imipramine and methylphenidate showed that they were comparable, but imipramine had a superior effect on sleep. Amphetamine-like drugs raise the level of noradrenaline in the blood, and tricyclics which block reuptake of noradrenaline have a similar effect on the CNS. The role of the noradrenaline pathways in the coping mechanism in the brain has been discussed, so it is not surprising that these two groups of drugs have been used in hyperactive children. By school age, the attention deficit leads to demands for treatment, if only to decrease disruption in class.

Some years ago, a number of young women presented at my clinic with features suggesting a stress disorder. It was soon clear that they were suffering from severe sleep loss from the hyperactive child at home. Helping the mothers required treating the children. Having treated teenagers for dependence on amphetamine, I was loathe to use methylphenidate. They were treated with amitriptyline in the form of syrup. About twelve patients in all, in the second to fourth year of age, were so treated in dosages of 1 to 2 mg/kg. Occasional children required higher doses to enable them to sleep reasonably, and when the dose approached 3 mg/kg they were also given sodium valproate (20 mg/kg) to prevent the fits which have been described with imipramine doses of 5 mg/kg.

Mothers had to be trained not to use repeated stimulation with moving objects, bright lights, etc. to keep them quiet. Such activities raise arousal level in the brain, and when fatigue eventually sets in the sleep produced is of short duration. Corcoran has described how sleep deprivation lowered coping ability in extraverts but seemed to raise arousal and efficiency in introverts. Normally, the introverts ran their lives at the peak of the inverted-U curve relating efficiency to arousal, but extraverts were part-way up the ascending portion of the curve. Our studies of compulsive behaviour in relation to anorexia indicated to us that introverts are often perfectionists and drive themselves excessively, sometimes using sleep deprivation to increase coping over short periods.

After six months of stable state, gradual reduction in the dose of amitriptyline was started. A plastic syringe to measure the dose accurately was a great help to the mothers. All the children treated were weaned off amitriptyline in one to three years with no relapse. Some needed a small increase in dosage on going to nursery or ordinary school, and the mothers were advised to lessen stimulating activity after they came out of school for a while.

Although there is a high resistance to the use of Ritalin in this country, it would be helpful to many