LETTERS TO THE EDITOR

Preference is given to letters commenting on contributions published recently in the *JRSM*. They should not exceed 300 words and should be typed double spaced

An NHS Staff College?

I write as a recently retired chairman of a health authority to give partial support to Duncan Smith's proposal (May 2000 *JRSM*, pp. 217–218) that a Staff College is needed for the NHS, providing one-year courses for leading young doctors, nurses and managers working together. Secondly, the Staff College would organize programmes of seminars and workshops for senior leaders of the same professions to cooperate on solutions to particular problems—or wide issues, I suppose—confronting health services at that time. These groups could then give valuable and independent advice to politicians and the NHS Executive, Duncan Smith thinks.

The key characteristic of the two levels is that the participants in both would all be professionals working in the NHS already, so would bring practical knowledge to the discussions and the solutions that emerge. My first reservation is that if all were from that source, they would tend to bring vision of their local trees to discussions, but not of the forest. A fair percentage of professions with 'overview' skills should participate at both levels of the Staff College, and civil servants too. The overall value would presumably be the non-political, or at least balanced political, nature of the College's output at both levels.

A second reservation is that the usefulness of such 'independent' advice to the effective management of the NHS is not proven. What is needed is a powerful individual to take up the idea with a small group to explore its value to the NHS and thrash out the details of the proposal. It would be best if that were done under the aegis of one of the privately endowed foundations, trusts or colleges—for the only other likely financial sponsor would be government, and that would destroy the non-political character of the proposal at the start.

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Comparative medicine of senescence

Mr Lavery (June 2000 *JRSM*, pp. 296–298) rightly emphasizes the importance of comparative studies of biological processes relevant to human disease. In particular, preoccupation with rodent models can be very misleading and a solitary focus on humans is dangerously narrow; humans, despite their unique attributes, are animals and have not shed vital characteristics either of primates or of mammals. Strangely, in this article as in many others, there is no mention of the unique attributes of the dog for the study of processes relevant to the clinical biology of disease, and of multifactorial diseases in particular[1].

The dog, within a single species, presents enormous phenotypic diversity exemplified by breeds spanning a 40-fold range of bodyweight, with huge differences in shape, athleticism and disease patterns, including large differences in blood pressure and susceptibility to cardiovascular disease, tumours and so on. Yet breed diversity rests on genetic homogeneity greater than that between human ethnic groups. Pet dogs, as studied in veterinary clinical research, offer unique insights into multifactorial diseases in particular, since these are inherently difficult to model. Thus, for example, on the question of the role of diet in the progression of chronic renal failure, dogs would have afforded clearer insights than rodents into the human situation[2]. Dogs have further advantages in the study of diseases where prenatal events may govern adult clinical destiny, for example in cardiovascular disease, since their gestation, maturation and lifespan are short compared with humans, multiparity is usual and both breeding and diet are readily subject to control. Thus dogs can provide models which combine ethical acceptability with biological authenticity, including environments shared with humans (e.g. with regard to allergens, toxins and carcinogens). These opportunities will proliferate as the range of minimally invasive techniques available to veterinary clinical research increases.

Finally, with regard to longevity, similar breeds show fascinatingly different lifespans in the absence of obvious relevant diseases differences. The very fact that some breeds are senescent at 6 years while others are flourishing at 12 offers a clear opportunity to test some of the current concepts concerning the biological control of ageing[3].

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Paediatric research

While one must congratulate Dr Tim Chambers (June 2000 *JRSM*, pp. 320–321) on his excellent dialogue about the ethical dilemmas relating to clinical research in paediatrics (in happy contrast to the pronouncements of self-appointed 'experts' on the question) I wonder whether he has sufficiently stressed the implied bargain between us and the parents whom we exist to serve, based on exchanging the benefits that their children gain from previous research for the possible benefit to future children afflicted by illness likely to be derived from further study. It is not as if we

ever know for certain that the way we treat illness now is necessarily effective or even harmless as many examples make clear; that is why physicians should be educated rather than trained.

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Placebo analgesia

The paper by de Craen *et al.*[1] and subsequent correspondence[2] have referred to the possible role of endogenous opioids in the mechanism of placebo analgesia, drawing on the study by Levine and his colleagues[3]. Since the article by Levine *et al.* was published in 1978 it has become clear, however, that the explanation for placebo analgesia is much more complex than that suggested by their study. Using an experimental paradigm very similar to that utilised by Levine *et al.*, Mihic and Binkert[4] were not able to replicate the reversal of placebo analgesia by naloxone. Indeed, they found that the administration of naloxone 'increased the intensity of placebo'. In a subsequent study, Grevert and her colleagues found only a partial reversal of placebo analgesia by naloxone[5] and suggested that non-opioid mechanisms contribute.

A brief review by ter Riet *et al.*[6] of six studies into possible mechanisms of placebo analgesia in man concluded only that 'placebo analgesia may exist' and that endogenous opioids 'play a role in the mechanism'. Reversal of placebo analgesia by naloxone reached statistical significance in one out of three studies of experimental ischaemic arm pain in healthy volunteers, and in two out of three studies of postoperative pain (including the study by Levine *et al.* referred to above). The work of Mihic and Binkert was not included. A more recent study by Amanzio and Benedetti[7] has suggested that the mechanism of placebo analgesia may be dependent on the method used to elicit the placebo response, and that placebo response elicited by conditioning has a different mechanism from that elicited by cognitive factors.

In my view, however attractive such an explanation may be, it is too early to conclude that the phenomenon of placebo analgesia can be fully explained by the release of endogenous opioids, and there is even less support for the hypothesis that other forms of the placebo effect can be explained by such a mechanism.

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5 Grevert P, Albert LH, Goldstein A. Partial antagonism of placebo analgesia by naloxone. *Pain* 1983;**16**:129–43

6 ter Riet G, de Craen AJM, de Boer A, Kessels AGH. Is placebo analgesia mediated by endogenous opioids? A systematic review. *Pain* 1998;**67**:273–5

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Bubonic plague in biblical times

Discussing seventeenth century treatments for bubonic plague Dr Holland (June 2000 *JRSM*, pp. 322–324) states that the disease was unknown in classical times. It was however known in biblical times. In the fifth chapter of *1 Samuel* the capture of the Ark of the Covenant from the Israelites by the Philistines at the battle of Aphek was followed by the outbreak of what appears to be plague in the five cities of the Philistines starting in Ashdod. The New International Version (NIV) in its footnotes records that the Septuagint (a translation from the Hebrew to Greek done in Alexandria for Ptolemy Philadelphus) and Vulgate (a translation by St Jerome into Latin from the Septuagint) texts elaborate on the fact that Philistines were smitten with tumours as follows. In *1 Samuel* 5 v 6 the NIV states the Philistines were afflicted with tumours and the Septuagint and Vulgate expand this point with the words 'and rats appeared in their land, and death and destruction were throughout the city' and in v 9 of the same chapter the Septuagint versions expand 'He afflicted the people, both young and old with an outbreak of tumours' by specifying the site of the tumours as being 'in the groin'.

The Philistine rulers and their priests decided to send the Ark of the Covenant back to Israel, and on the advice of their priests (*1 Samuel* 6 v 4) provided a guilt offering of 'five gold tumours and five gold rats according to the number of the Philistine rulers of their cities'. The priests advised (v 5) 'make models of the tumours and of the rats that are destroying the country and pay honour to Israel's God'.

It therefore appears that plague with its associated buboes was known in ancient times and an association with rats established.

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Insulin coma therapy for schizophrenia

Dr Crammer asks (June 2000 *JRSM*, pp. 332–333), 'Does insulin in high doses have a direct effect on some neurons and the balance of brain functions (some neurotropic factors

are also ''insulin-like''?)' Recent work on the role of insulin in the brain suggests that the answer may be 'yes'. Neurons synthesize and release insulin. As glucose utilization in neurons is largely insulin independent, this suggests that insulin in neurons has some other functions. These are listed by Man *et al.* as growth, maturation, protection, neuromodulation, learning and memory. Insulin recruits GABA and other receptors to the postsynaptic domain, and the rate of constitutive dynamin-dependent endocytosis of AMPA receptors is accelerated by insulin. Any one of these effects might be of relevance to the reported therapeutic effect of insulin therapy in schizophrenia, in which the high dose of insulin may be more important than the hypoglycaemia or the coma.

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Emergency management of meningitis

At the end of their review (May 2000 *JRSM*, pp. 225–229) Dr Heyderman and Dr Klein state that 'the majority of patients with meningitis in the UK have meningococcal disease'. If this is the case, surely the title of the article should not refer specifically to meningitis. Meningococcal disease can manifest itself as meningitis or septicaemia[1] and is caused by the bacterium *Neisseria meningitidis*. This presents in 50% as meningitis, in 10% as septicaemia alone and the two presentations coexist in 40% of cases[2,3]. This differentiation is important as the case-fatality of meningococcal septicaemia is tenfold that of meningococcal meningitis which is generally less than 5%[2]. The emphasis of the article is on emergency management, but surely part of the emergency is the possibility of septicaemia. This vital distinction might help reduce the unwitting reference to 'meningitis' when in fact a different condition is being suspected, where there may be an absence of symptoms and signs of meningitis. Should meningococcal septicaemia perhaps be given a different name other than the broad umbrella term 'meningitis'? This could help to alert parents and doctors to suspect the possibility of septicaemia in children who present with an unresolving history of being 'unwell and pyrexial without an obvious source' ('UPWOS')[4].

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4 Charlton R. Let's be clear about what 'meningitis' is [Letter]. *Doctor* 27 April 2000:38

Ronald Ross

This month in history

Although his interests spanned from languages and mathematics to writing drama, novels and poetry, it was his tryst with a mosquito that won Ronald Ross (1857–1932) international acclaim. Ross entered the Indian Medical Service in 1881 and in ensuing years became interested in malaria. In 1888, he received a diploma in public health and took a course in bacteriology in England. Upon returning to India, he embarked on research in malaria. Laveran had shown that blood of malarial patients contained the minute pigmented bodies of the parasites and Manson had proposed that mosquitoes transmitted the disease. To prove Manson's hypothesis, Ross had to contend with not only a variety of mosquitoes but also a variety of malarial parasites. He learned to dissect and examine mosquitoes. The key to the problem was finding the correct mosquito. Ross found and bred *Anopheles*, fed them on malarial patients and killed insects on different days to study changes. On 20 August 1897, Ross saw a mass of cells with a circular outline and pigment granules in the stomach of mosquito no. 37, which had been fed on 16 August. The observations were confirmed on other mosquitoes. On 20 August 1897 ('Mosquito Day'), Ronald Ross had proved to the world that the *Anopheles* mosquito was the carrier of the malarial parasite.

Venita Jay