

WHO ANALGESIC LADDER

Sir,

I wish to make several observations on the paper 'Aspects of pain management in the older person' (Tan HN, Leong IYO. *J R Coll Physicians Edinb* 2008; 38:148–53). The authors refer to the World Health Organization analgesic ladder. But this refers specifically to cancer pain relief, which, in fairness to the authors, is widely misused by the profession as if it were a guideline for treatment of pain of all types.

Doctors often seem to have a remarkable tolerance for pain experienced by others. If I, no matter what my age, have a pain (whatever the cause and whatever the duration) I want the priority to be relief of that pain as soon as possible. Specifically I do not want to ascend a ladder until effective analgesia is achieved. I want my doctor to start off by giving me what he or she judges will be effective and safe analgesia and then seeing if we can descend the ladder of analgesia.

There are important but neglected ways in which pain can be alleviated. In the past physiotherapists had to stop using ethyl chloride skin counterirritant sprays on footballers who seemed to have leg cramp, because some were then able to play on despite having fractures. Years ago, as a junior doctor, while waiting for a diamorphine injection to be drawn up, I sprayed ethyl chloride on the skin areas deep to which a patient with myocardial infarction was experiencing pain. This relieved pain immediately without side effects. Perhaps use of similar initial instant, albeit short-term, forms of analgesia should be investigated. In the event my seniors told me off!

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Authors' response

We thank Dr Welsby for his letter. He has made several important points.

We are aware that the World Health Organization analgesic ladder was developed in 1986 for cancer pain relief. However, over the years, it has been widely used because it is a simple, concise and safe tool to help physicians manage pain symptoms in their patient. Its use has been validated in patients with end-stage renal failure in a study by Barakzoy et al,¹ suggesting that its use extends beyond cancer pain. We also find that it is a useful teaching instrument for beginners in pain management, although it has its limitations in the non-cancer pain arena. Our belief is that the ladder has to be supplemented by disease- and pathology-specific interventions as well. For example, our approach to pain in patients with osteoporotic vertebral fractures would include pharmacological interventions such as calcitonin, bisphosphonates and interventional measures such as vertebroplasty or epidural

injections. Lastly, the analgesic ladder is in line with general geriatric prescribing principles.

Dr Welsby suggests that the aim of management should be the relief of pain by starting higher on the ladder and de-escalating with time. The bulk of our article was focused on the management of chronic pain in the older person, as this is the main type of pain reported by older people. While Dr Welsby's suggestion would be applicable in acute pain, this is often not the possible in chronic pain for a number of reasons. From the published trials, the evidence points towards partial relief at best for any analgesia or adjuvant, even strong opioids. In a study by Maier et al.,² only about one third of patients responded to a fairly large dose of opioids (up to 180 mg/day of morphine), with half of the rest being partial responders and the other half non-responders.

Starting higher up the ladder does not assure pain relief. It is also not always possible to identify the most appropriate medication for a particular pain. This has been demonstrated by the study by Nikles et al.,³ which used multiple N-of-1 trials comparing NSAIDs with paracetamol for patients with pain from osteoarthritis. In their study, 65% of patients changed the type of medication they were on following the N-of-1 trials. The proportion who responded to paracetamol were comparable to those who responded to NSAIDs. Lastly, many regulatory bodies make strong opioids unavailable to general practitioners. However, weak opioids and tramadol are widely available, and sometimes can be dispensed by pharmacists without a doctor's prescription. Thus regulatory frameworks do naturally result in drug use according to the ladder in such countries.

We acknowledge there are many ways to relieve pain. Practising in a traditional Asian society, we are exposed to methods ranging from the use of traditional herbal remedies to cupping and acupuncture. However, the evidence for many of these modalities are minimal or, at best, point towards pain relief during the course of the treatment. We are aware that one can reduce the pain of myocardial infarction with ethyl chloride. One of us has reduced pain from spinal and epidural metastases for a period of nearly a week by using trigger point desensitisation. However, these practices can only be used carefully in an overall plan. Lastly, Dr Welsby's anecdote reminds us of the necessity to both relieve pain and seek an underlying cause where possible at the same time.

References

- 1 Barakzoy AS, Moss AH. Efficacy of the World Health Organization analgesic ladder to treat pain in end-stage renal disease. *J Am Soc Nephrol* 2006; 17:3198–203.
- 2 Maier C, Hildebrandt J, Klinger R et al. Morphine responsiveness, efficacy and tolerability in patients with chronic non-tumor associated pain – results of a double-blind placebo-controlled trial (MONTAS). *Pain* 2002; 97:223–33.

- 3 Nikles CJ, Yelland M, Glasziou PP et al. Do individualized medication effectiveness tests (n-of-1 trials) change clinical decisions about which drugs to use for osteoarthritis and chronic pain? *Am J Ther* 2005; 12:92–7.

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Editor's note: Please also see JS Kelly's clinical opinion on vapocoolants, ethyl chloride and cryoanalgesics, p. 232.

OBESITY, INFERTILITY, ABUNDANCE AND SPACE

Sir,

In their paper on obesity and infertility (*J R Coll Physicians Edinb* 2007; 37:321–4), Dr Zachariah and Dr Acharya stressed visceral (abdominal) obesity and the associated insulin resistance; a likely reflection on their practice in reproductive medicine. Both abdominal obesity and insulin resistance appear to be aetiologically related and are commonly encountered in both polycystic ovary syndrome (PCOS) and metabolic syndrome (MS).¹ However, apart from the introductory remarks, Table 2 and the 'redundant' Table 1, the article is almost entirely confined to PCOS and its associated manifestations. Yet the diagnostic criteria of PCOS (Table 3) do not include obesity or overweight. In truth, the prevalence of overweight, including obesity, among women with PCOS (~ 50%), as the authors state, is similar to that in the general population.² Moreover, the authors also remarked that 'many obese women remain fertile'. It may even be argued that if the resumption of ovulation and fertility follows a weight reduction in PCOS of as little as 5%, some other factor has contributed to the resumption of ovulation.

The recent obesity epidemic, or even pandemic, appears to have been accompanied by a semi-epidemic prevalence of MS and PCOS (at least 23% and 5% respectively). The characterisation of MS in 1988³ is a likely testimony of its recent flare-up. Likewise, PCOS appears to have been scarce, at least until the publication in 1962 of a meta-analysis of 187 reports on 1,079 surgically proven PCOS cases, with a mean average of <6 patients per report,⁴ whereas nowadays the inclusion of >400 PCOS patients in a single study is not unusual.¹

In the same issue of the *Journal*, Professor Seaton's remarkable transdisciplinary paper encroached on Malthusian theory, which links plentiful food resources with population growth (Seaton A. Galen, Gaia and global climate change: Harvey and the history of air. *J R Coll Physicians Edinb* 2007; 37:357–61). As obesity is evidence of abundance of food, the association of obesity with infertility contradicts Malthusian theory, at least superficially.

Professor Seaton also remarked on the earlier easy existence in the 1950s and 1960s, which he ascribed to

the relatively lower energy consumption in those decades. But another mechanism deserves mentioning. Worldwide, migration, once open especially to the Americas and Australasia, declined precipitously during the first half of the twentieth century to an almost complete cessation before the century's close. For Britons, migration remained a 'safety valve' and a safeguard against an overpopulated state. But this safety valve has been squeezed more and more, and by the early 1970s had probably lost its effectiveness, coinciding with the flare-up of MS and PCOS in particular and the pandemic of obesity in general.

Modern medical literature underestimates psychological factors, particularly when dealing with 'psychosomatic' disorders with measurable physical manifestations, as has been partly expressed in the *Journal* recently.⁵ As a result, we commonly read 'the cause is poorly understood'; contradictory results on treating such disorders are not unusual as exemplified by PCOS.⁶ When lifestyle changes are blamed for causing obesity and MS, they are translated only into dietary factors and physical inactivity.

However, another likely contributor – the psychoneuroendocrine interactions with the lifestyle of the individual – is ignored. The psychology of immigrants seeking better living conditions differs from that of those who cannot migrate, not to mention the psychology of the desperate Pima Indians encaged within a colony in Arizona. It is likely that the seven PCOS cases reported by Stein and Leventhal in 1935⁷ could have been aetiologically related, at least partly, to the almost coincident Great Depression of 1929–33. We may elaborate that the associated unemployment and financial difficulties triggered the mechanism that hindered reproduction – the 'anovulation of PCOS'.

Personally, I have witnessed approximately ten fowls in a hen house of about 6 m² for more than one year. None of the fowls displayed hatching behaviour. But when the hen house was expanded to about 50 m², a mass yearning for hatching followed almost immediately. Both humans and fowls appear to follow some biological 'instinctual' mechanism somewhere between the hypothalamus and the limbic system. The association of depressive illness with the hyperactive hypothalamus's 'pituitary–adrenal axis' has been well documented.⁸ The abdominal obesity that Zachariah and Acharya overstressed probably bespeaks the central hyperactivation of this axis akin to the obesity of Cushing's disease.

To conclude, the aetiology of the recent epidemic of obesity and the associated MS and PCOS requires, in addition to studies of diet and sedentariness, an exploration of the effect of psychology on neuroendocrine mechanisms; the associated infertility could also be through some central mechanism. A recent report shows the reward of

the proper evaluation of psychological factors.⁹ Malthusian theory warrants ascribing population growth to the abundance of land (Gaia's territory) in addition to the abundance of food supply.

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References

- 1 Barber TM, McCarthy MI, Franks S et al. Metabolic syndrome in polycystic ovary syndrome. *Pol J Endocrinol* 2007; 58:34–41.
- 2 Summerton C, Shetty P, Sandle LN et al. Nutritional, metabolic and environmental disease – obesity. In: Haslet C, Chilvers ER, Boon NA, editors. *Davidson's principles and practice of medicine*. 19th edition. Edinburgh: Churchill Livingstone; 2002. p.301–6.
- 3 Reaven GH. Role of insulin resistance in human disease. *Diabetes* 1988; 37:1595–607.
- 4 Goldzieher JW, Green JA. The polycystic ovary. I. clinical and histologic features. *J Clin Endocrinol Metab* 1962; 22:325–38.
- 5 Ong HT, Boon N. Stress and the heart – conflicting views. Letter to the editor and author's response. *J R Coll Physicians Edinb* 2006; 36:93–4.
- 6 Legro RS, Barnhart HY, Schlaff WD et al. Clomiphene, metformin or both for infertility in the polycystic ovary syndrome. *N Eng J Med* 2007; 356:551–66.
- 7 Stein IF, Leventhal ML. Amenorrhoea associated with bilateral polycystic ovaries. *Amer J Obstet Gynecol* 1935; 29:181–91.
- 8 Saeed AK, Al-Dabbagh TQ. Type 2 diabetes and its association with hypertension and depression in an Iraqi population. *Ann Saudi Med* 2003; 23:254–9.
- 9 Bryant R. Disentangling mild traumatic brain injury and stress reactions (editorial). *N Engl J Med* 2008; 358:525–7.

Author's response

This paper was commissioned as part of the College's contribution to CME and written within strict guidelines. Therefore, we could not include a detailed discussion of the effects of obesity on fertility. However, we thank Dr Al-Dabbagh for the opportunity to expand on our remarks. In the first paragraph of his letter it appears that he has missed the point that the distribution of fat is all important. It is the visceral fat that causes the problems. If the distribution of fat is subcutaneous then it is likely that an obese person would not be infertile. As regards PCOS, although the definition does not include obesity, the effects of visceral fat are expressed biologically and this is, in part, the definition. There is now evidence that weight loss helps, so it is difficult to argue against that evidence (for instance, see the recent review by Lash and Armstrong¹).

In the fifth paragraph Dr Al-Dabbagh discusses the issue of differing results from differing treatments. It is well known that initial trials in many treatments are encouraging, but subsequent results do not bear out the initial promise. This could be as a result of accumulating more knowledge and patient numbers as the number of trials go up, but also the effect on subgroups with the same disease. For example, in PCOS we could have patients who have polycystic ovaries and hyperandrogenemia (HA) in one profile and HA and associated clinical symptoms in another. These two groups may give differing results. It is, therefore, quite understandable that the effects of metformin on PCOS patients (to which Dr Al-Dabbagh refers) are different in the initial studies.

We do not think the rise in obesity (initially in developed countries and now in other countries) can be put down to immigration as the numbers would not add up, and obesity far outstrips immigration in developed countries.

- 1 Lash MM, Armstrong A. Impact of obesity on women's health. *Fertility and Sterility*. In press. Online publication: 14 April 2008. Available from: <http://www.sciencedirect.com/science/article/B6T6K-4S8TRBR-B/1/2aee3c4968de6161272458f18695fb79>

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I thank Dr Al-Dabbagh for his thoughtful comments and for paying me the compliment of having thought about my article, which was an attempt in a short space to trace the science behind global climate change back to the scientific revolution in the West, epitomised by William Harvey. In parenthesis, it is worth pointing out that the circulation of the blood was postulated in the thirteenth century in the great period of Islamic science, by Ibn an-Nafis.

Population growth is, of course, central to the current global climate and food crisis and the observations in Malthus's eighteenth-century essay are still relevant to the plight of those currently suffering from shortages of rice and wheat. I don't think availability of land or oversupply of food leading to obesity were seen by him as problems, and as far as I can recall he did not mention them in his essay, however prescient he was otherwise.

It is one of the ironies of globalisation that obesity and want exist side by side in the world today and both are considered to constitute international health crises. One of the many steps that I mentioned in my lecture as essential to the amelioration of the climate crisis is a global modification of food production, distribution and consumption practices towards sustainable agriculture and away from meat eating.

The aim of my lecture was to inform colleagues of these issues and to stimulate thought as to what we, individually and collectively, could do about them. I am grateful to Dr Al-Dabbagh for giving me the opportunity of reiterating this.

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Correction: Falls in the elderly

The penultimate paragraph in KE Anderson's paper, Falls in the elderly (*J R Coll Physicians Edinb* 2008; 38:138–43), should have read: 'Initial reports of hip protectors in hip fracture prevention were promising in cluster randomised trials in institutional settings, but more recent randomised controlled trials have failed to confirm their benefit.'