

mortality, while such an effect did not occur for the elder group.<sup>6</sup> One should also study the possibility of interactive effects of biomedical and psychological factors. There are several examples of biomedical risk factors increasing or decreasing the influence of psychological variables. One of these studies showed that in the group who smoked at least 25 cigarettes a day, depressed people had a 4.5 times higher chance of developing cancer than the non-depressed people who never smoked. The relative risk of depression was even as high as 18.5 for lung cancer and other cancers at sites associated with smoking.<sup>7</sup>

Hansen and co-workers did an excellent study with a large sample size, long follow-up, and control for confounders. Their work was based on data from a population-based twin registry and included 1898 cancer cases. Mean follow-up was 25 years. Analyses were adjusted for several relevant confounders, especially age, sex, early environmental and genetic factors, cigarette smoking, alcohol consumption, exercise, diet, and body mass, and, for hormone-related organ cancers, use of oral contraceptives and nulliparity. One minor comment concerns the fact that they have dichotomised all health-behaviour variables, such as tobacco use, which was divided into current smoker or not. However, it is unlikely that their findings would have changed substantially if these control variables had been divided into more categories.

Hansen and co-workers convincingly show that extroversion and neuroticism are not predictive for later

initiation of cancer, which is in line with the conclusion of our review.<sup>3</sup> These risk factors were not important for cancer initiation in interaction with smoking, and nor was the joint effect of extroversion and neuroticism significant.

What does all this imply for future research? After dozens of longitudinal studies, one could decide to stop putting any new effort into this research line. If not, research should focus on psychological factors for which at least some evidence has been found: the tendency towards helplessness when confronted with stressful conditions, repression of negative emotions, and minimising the impact of the disease.<sup>3</sup>

*Bert Garssen*

Helen Dowling Instituut, 3582 JJ Utrecht, Netherlands  
bgarssen@hdi.nl

I declare that I have no conflict of interest.

- 1 Hansen PE, Floderus B, Frederiksen K, Johansen, C. Personality, health behavior and risk for cancer: a prospective study of a Swedish twin cohort. *Cancer* 2005; **103**: 1082–91.
- 2 Faller H, Lang H, Schilling S. Cancer-prone personality as a causal attribution: an expression of the spread of a maladaptive disease. Kausalattribution "Krebspersönlichkeit"—ein Ausdruck maladaptiver Krankheitsverarbeitung? *Z Klin Psychol Psychiatr Psych* 1996; **44**: 104–16.
- 3 Garssen B. Psychological factors and cancer development: evidence after 30 years of research. *Clin Psychol Rev* 2004; **24**: 315–38.
- 4 Schwarz R, Geyer S. Social and psychological differences between cancer and non-cancer patients: cause or consequence of the disease. *Psychother Psychosom* 1984; **41**: 195–99.
- 5 Schwarz R. Psychosoziale Faktoren in der Karzinogenese: zur Problematik der sogenannten Krebspersönlichkeit. *Psychother Psychosom Med Psychol* 1993; **43**: 1–9.
- 6 Schulz R, Bookwala J, Knapp JE, Scheier M, Williamson GM. Pessimism, age, and cancer mortality. *Psychol Aging* 1996; **11**: 304–09.
- 7 Linkins R W, Comstock GW. Depressed mood and the development of cancer. *Am J Epidemiol* 1990; **132**: 962–72.

## Doping and the child: an ethical policy for the vulnerable

On April 1, 2005, the American Academy of Pediatrics (AAP) published a policy statement on the use of performance-enhancing substances.<sup>1</sup> The statement questions several assumptions about the so-called drug war in sports and how it might be won. It argues for a more restrictive ethical framework that takes into account the most vulnerable group it affects—children. The proposal calls for greater responsibility from health-care professionals by drawing attention to the wider concerns about care in public health that surround the use of performance-enhancing substances: "A significant number of adolescents who are

not involved in competitive athletics use performance-enhancing substances."<sup>1</sup>

Framing the drug war in sport as a public-health issue has received renewed support in recent months. In the USA, the debates about the Bay Area Laboratory Co-operative and unknown designer steroids have led to further political support to tackle the problem of doping. In his 2004 State of the Union Address, President George W Bush spoke of the danger of steroids in sports and the need for sports organisers to "take the lead and send the right signal" to young people.<sup>2</sup> Moreover, the congressional hearings on Major

League Baseball have reinforced the political momentum on tackling substance abuse. The prospect of drug-testing protocols for sports programmes in US high-schools is a further indication of this momentum. However, the AAP is doubtful that such a strategy would be effective: "Drug testing and legal sanctions are intended to be deterrents but have little effect on most children and adolescents involved in sports."<sup>1</sup>

The AAP statement reinforces the poorly defined role of health-care professionals within sports. Whilst the AAP is unequivocal about the health-care providers' responsibility—health, not performance—the statement does not grapple with the challenges faced by professionals working with athletes, nor does it address how the integrity of a physician's judgment might be protected within that environment. A sports physician might struggle over deciding whether the athlete/patient is entitled to reparative care, if its purpose is to return them to competition. Are the athlete's interests best served by fixing them for competition, or by advising them to rest?

Yet this complexity might suggest a reconsideration of how a physician relates to the athlete, a special kind of patient perhaps. One might argue that greater ethical limits must be placed on the use of medicine in sport and athletes' autonomy, because an athlete's decisions might be influenced considerably by the pressures to perform, especially when so much is often at stake for an athlete in every major performance. This coercive environment can inhibit an athlete's autonomous choice to reject the use of performance-enhancing substances. When treating minors, this problem is exacerbated and the AAP claims that anti-doping policy needs to reconsider its priorities, placing the potential and real harm to children at its centre.

The AAP statement identifies that anti-doping policy does not distinguish between different kinds of user, which poses big challenges to the world of elite sport. Moreover, it indicates a need for greater collaboration between drug companies and anti-doping authorities, because anti-doping authorities rely on drug companies to know what new products might be arriving on the market that athletes could obtain. Knowledge of new products is essential to ensure that new methods of detection are developed with a good lead on the cheats. However, the financial incentive for drug companies is limited, because they make money from muscle

**Rights were not granted to include this image in electronic media. Please refer to the printed journal**

boosting of athletes. Similarly, whilst more rigorous links with scientific and medical research would be of great assistance to the world of sport, non-sport scientists do not have much of an interest in sport unless the funding relates to some greater medical insight; so their incentive is also limited.

Nevertheless the statement beckons a re-definition of anti-doping strategies, which should take into account the wide range of performance-altering technologies available to athletes, beyond the lists of banned substances. For example, the latest scandal concerns the ethics of "blood spinning", a form of blood manipulation, which has been proposed by Chelsea soccer club physician Bryan English, as a method of promoting rehabilitation when injured.<sup>3</sup> Similarly, the use of hypobaric chambers to simulate higher altitudes and allow an athlete to train harder remains legal for the moment, but it is under review by the World Anti-Doping Agency.<sup>4</sup>

The message from the AAP places a broader requirement on anti-doping strategies to be made publicly accountable and subject to greater ethical scrutiny. A significant part of this strategy aims to promote ethical debate. The AAP notes that health-care professionals cannot discourage misuse merely by scare tactics or denying known performance-enhancing effects of banned substances. Rather, education must engage young people with the morality of sport, promoting public engagement with ethics. Whilst young people might fully understand the health risks of substance abuse, cultivating a moral view on science and medicine does not arise solely from having facts about health risks.

Andy Miah

University of Paisley, Ayr Campus, Paisley KA8 0SR, UK  
email@andymiah.net

I declare that I have no conflict of interest.

1 American Academy of Pediatrics. Policy statement: use of performance-enhancing substances. *Pediatrics* 2005; **115**: 1103–06.

2 Bush GW. State of the Union Address. Washington DC. The White House. 2004: <http://www.whitehouse.gov> (accessed Feb 24, 2005).

3 Goodbody J. Chelsea escape bloody nose. *The Times (Lond)* May 6, 2005: <http://www.timesonline.co.uk/article/0,,27-1600167,00.html> (accessed May 10, 2005).

4 Shipley A. Speedskaters live the high life in oxygen-thin rooms. *Washington Post* Dec 15, 2004: <http://www.washingtonpost.com/wp-dyn/articles/A64840-2004Dec14.html> (accessed Apr 22, 2005).

## Bat rabies—the Achilles heel of a viral killer?

In October 2004, in Wisconsin, USA, a 15-year-old girl was diagnosed with rabies after being bitten by a bat a month before the onset of symptoms. Surprisingly, and fortunately, she survived. It is the second reported survival of rabies after a bat bite. The first patient was a 9-year-old boy in Ohio, USA, who received prompt treatment with rabies vaccine after being bitten on the thumb by a rabid big-brown bat.<sup>1</sup> The Wisconsin case is unique because the patient received no rabies prophylaxis. This exceptional survival addresses the question of the pathogenicity of bat rabies and whether or not bat rabies is the Achilles heel of one of the very few human infections with a near-100% mortality rate.

The causal agents of most human rabies virus infections in North America are rabies-virus variants that circulate in bats, especially silver-haired and Mexican free-tailed bats. Pathogenicity studies reveal that virus variants associated with silver-haired bats are less neurovirulent than canine (coyote) rabies-virus variants when administered intramuscularly.<sup>2</sup> The rabies virus of the silver-haired bat constitutes an attractive model to investigate the molecular basis of rabies-virus pathogenicity.

Faber et al<sup>3</sup> used a reverse genetic approach to dissect the rabies-virus pathogenicity of the silver-haired bat. They identified, among the six virus genes—N, P, M, G,  $\psi$ , and L—those that can be replaced by genes of a totally non-pathogenic rabies virus to generate viral attenuation. Chimaeric mutants were obtained by replacing the bat rabies-virus genes, one after the other, by the corresponding genes of the non-pathogenic rabies virus. Pathogenicity of the silver-haired bat's rabies virus, of the non-pathogenic rabies virus, and of the four chimaeric rabies viruses for the L gene, L+ $\psi$ , L+ $\psi$ +G, and L+ $\psi$ +G+M, respectively, were compared by recording mortality after mice had been injected intramuscularly. Whereas mouse mortality was 100% after intramuscular injection of the rabies virus, mortality was reduced by 40% when L and  $\psi$  were replaced, and by 90% when G was additionally replaced. Additional loss of the M gene restored the parental phenotype of the non-pathogenic rabies virus, with 100% survival.

These experiments identify L+ $\psi$ +G as the combination of bat rabies-virus genes whose replacement by genes of the non-pathogenic strain confers almost complete attenuation. Contribution of L to attenuation is low because the chimaeric L mutant gains only 10% survival compared with parental rabies virus from the silver-haired bat. The role played by  $\psi$ , the most divergent genomic area of rabies virus, is intriguing, since it is not transcribed and its absence did not modify rabies-virus multiplication in the nervous system.<sup>4</sup> The major role played by G in attenuation confirms that G of the rabies virus, a 505 aminoacid type I membrane glycoprotein with three potential N-glycosylation sites, plays a pivotal role in several aspects of rabies-virus physiology. G is indeed responsible for the attachment of the rabies virus to target cells, and confers to the virus the property to be transported retrogradely into the central nervous system.<sup>5</sup> G of the rabies virus plays a major role in neuronal death

**Rights were not granted to include this image in electronic media. Please refer to the printed journal**