Editor’s Choice

‘Knowing is not enough; we must apply. Willing is not enough; we must do.’

Jane E Ferrie

Many of us will be familiar with the above quote, widely attributed to Goethe, but few will manage to rise to its lofty call. Two men who did—Professor Mervyn Susser and Professor Tony McMichael, died recently and our discipline is the less for their parting.

Epidemiologist and epitome of integrity—Mervyn Susser

Goethe’s call to arms recurs in appreciations of Mervyn Susser. A celebration of his work in the International Journal of Epidemiology (IJE) in 2002 appeared under the title: Zena Stein, Mervyn Susser and epidemiology: observation, causation and action. At the end of his medical studies in South Africa, Susser and his wife, Zena Stein, ran a clinic in Alexandra township in Johannesburg. Although epidemiology was not yet on the medical curriculum, while there they carried out one of the first ever studies of community health in the developing world. It was published in the Lancet in 1955. Susser’s indictment of the appalling conditions of Black people and his increasing support for the struggle against apartheid led, a year later, to his relocation to the UK.

Gerald Oppenheimer, in his contribution to the celebration of Susser’s work, describes how a series of papers on the families of children with low IQ, published soon after their arrival in Manchester (UK), contain the important elements that characterized Stein and Susser’s research.

First is the belief that human health and disease are in large measure socially determined; they are deeply influenced by a community’s social relations, culture, and its institutions of medical care. Second is the commitment to elucidating or addressing social inequities or injustice, often as they are manifested and experienced as disease and death by segments of a population. Third is a conviction that their research ought ultimately lead to clinical, institutional and social policy changes.

In 1984, as South Africa approached a state of emergency and the struggle against apartheid intensified, Susser and Stein were instrumental in setting up the Committee for Health in Southern Africa (CHISA). CHISA was especially concerned about the disparity between medical care for Black and White patients, and about the direct effects of apartheid on health and mental health. Post apartheid, Susser and Stein continued to be politically and scientifically engaged in South Africa, particularly in relation to the HIV/AIDS epidemic which they fought to understand and contain, in their new home, the USA, as well as their old home. In all Susser’s work he strove to maintain the integrity of both his political views and his scientific values. Oppenheimer concludes it is a lesson worth noting. We note it and offer it as our tribute to an outstanding epidemiologist.

Eco-epi warrior—Tony McMichael

Tony McMichael suffered an unexpected and early death on the 26 September 2014. Only a few weeks before, he presented the opening Cruickshank Lecture at the IEA World Congress in Alaska on ‘Climate Change, the Anthropocene, and Human Health: Implications for 21st Century Epidemiology’ (http://ieaweb.org/).

McMichael’s early career as an epidemiologist focused on traditional environmental exposures, particularly exposures in the work environment. Rubber workers and those working with vinyl chloride were the focus of a tranche of early papers. Slightly later was to come important work on exposure to lead, both at work and in the general environment. McMichael’s work on lead is recognized as having...
been instrumental in the phasing out of lead in more than 100 countries, and it broadened his interest to exposures in the wider environment.

In February 1993, McMichael published a paper in the *IJE*: ‘Global environmental change and human population health: a conceptual and scientific challenge for epidemiology’. The paper laid out McMichael’s thesis that the ‘carrying capacity’ of the Earth’s natural systems was being overloaded by a set of problems arising from ‘the unprecedented combination of a huge and rapidly expanding population, resource-intensive industrial practices and land-exhausting agriculture.’ Essentially the paper provided a synopsis of the material to be published in much greater detail later the same year in his book *Planetary Overload: Global Environmental Change and the Health of the Human Species*. The book itself was rejected by a reviewer for Oxford University Press as being speculative and fantasy-like, but the then editor of the *IJE*, obviously more appreciative of the novelty and importance of the content, accepted the paper and published it as a ‘leading article’.

McMichael’s book *Planetary Overload* (Figure 1) was published by Cambridge University Press. It was to be pivotal to

Figure 1. Cover of Canto edition published 1995. Reproduced with the permission of Cambridge University Press.
Fittingly, McMichael lived to see the world’s greatest global climate change march to date. Getting the effects of climate change on human health onto the global agenda will be his lasting legacy.

Kropotkin

By the time he finished his doctorate, Tony McMichael had become fascinated by the ideas of the Pulitzer Prize-winning author and microbiologist Rene Dubos, and it was through writing to Dubos that he eventually secured his first postdoctoral position.6 In common with other thinkers on the ecology of health and disease, Dubos followed Peter Kropotkin (Figure 2) in emphasizing that the most important aspect of the natural world is not the law of the jungle or ruthless competition, but rather interdependence and co-existence, or mutual aid.8

The first ever mention of Kropotkin in the IJE was in a commentary last December on Edmund Parkes’ review of John Snow’s Mode of Transmission of Cholera: ‘History is not kind to critics. Its writers typically dismiss where they do not simply ignore those whose careful reviews argue caution in the face of works destined to become, in the future, classics. Think, here, Prince Peter Kropotkin whose naturalist studies focused upon the limits of Charles Darwin’s evolutionary theory and the direction in which research based upon it would be best directed’.9 In the Editorial for this December’s issue of the IJE, Tom Koch expands on this theme to provide an interesting and compelling exploration of the ideas presented in Kropotkin’s Mutual Aid: A Factor of Evolution,10 finding the evidence and concepts Kropotkin describes fundamental to the promotion of public health.11

Mutual Aid, published in 1902, is probably Kropotkin’s most famous work. Rarely out of print and often thought of as an anarchist classic, it actually comprises a series of articles Kropotkin wrote in reply to Thomas Huxley’s The Struggle for Existence in Human Society, published in the journal The Nineteenth Century. Kropotkin’s replies appeared in the same journal between 1890 and 1896 and were expanded to form Mutual Aid.10

Although Kropotkin was and is internationally recognized for his contribution to geography, Mutual Aid has generally been either dismissed or ignored, and Kropotkin labelled a crackpot. Partly this was due to his stance against Huxley and the then dominant interpretation of Darwin, but also because acceptance would have challenged those aspects of Social Darwinism carefully constructed to defend the interests of the ruling class and capitalist exploitation. Similar political agendas had underlined the earlier argument between Thomas Malthus and William Godwin, with Malthus recognized as a significant influence on Darwin and Darwinian thinking.11,12

Adopting the view presented in standard courses on evolutionary biology, Stephen J Gould similarly had always dismissed Kropotkin as daftly idiosyncratic. However, his view was challenged by the work of Daniel Todes published in a paper in the journal Isis in 1988 and in a book the following year.13 Todes’ work has been described as marking the beginning of Kropotkin’s rehabilitation,14 and Gould describes the effect of Todes’ analysis on his own view of Kropotkin in a Diversion that accompanies Koch’s Editorial.15 Several of the many scientific and pseudo-scientific criticisms of the premises in Mutual Aid have been shown to bear little weight.16 Koch’s Editorial points to recent support for Kropotkin’s ideas from research on the health effects of the social environment, and brings us right up to date with discussion of the implications of epigenetics in relation to thinking on natural selection.11
The other ‘Kropotkin’ Diversion—an excerpt from a longer piece on ‘The surplus population’ from a series of articles in Rollback magazine by Noam Chomsky—shows that the IJE has not been alone in ignoring Kropotkin’s work.17 We hope Koch’s attempt to focus epidemiological and public health attention on Kropotkin’s rather neglected contribution will promote further debate.

Environmental exposures

Seasonal variation in blood pressure has been long observed. Much of this research has been conducted in Western populations among whom access to good housing and health care ensures that such variation is mostly moderate. In this issue, Danting Su and colleagues report on the association between outdoor temperature and blood pressure in 60 000 rural participants in the China Kadoorie Biobank cohort screened over a period of 4 years. With little or no access to proper household heating in winter and temperatures as low as −3°C, much larger differences in blood pressure were observed between the coldest and hottest months than have been observed previously in Western populations: 19 mmHg for systolic and 8 mmHg for diastolic pressure.18

An Editorial in the February issue suggested that the burden of death attributable to hypertension over the next 20 years may substantially exceed that due to HIV/AIDS in low- and middle-income countries. The authors also drew parallels between the onset of the HIV/AIDS and hypertension epidemics in terms of lack of research, recognition and global health assistance.19 An analysis of data from the World Health Organization (WHO) Study of Global Ageing and Adult Health, published in the same issue, found high prevalence of hypertension but very low levels of control (average 10%) across the six low- and middle-income countries included.20 Possibly of greater relevance to the detection and clinical management of hypertension at the population level, Su and colleagues found hypertension detection rates to be more than twice as high in winter as in summer, but hypertension control rates nearly four times higher in summer than winter, although the proportion of the population on antihypertensive treatment varied little by season.18

Probably of little comfort to rural Chinese in the grip of winter, will be the lower risk of asthma, rhinoconjunctivitis and eczema usually associated with such environments. Existing evidence suggests that immigrants moving from less affluent countries to more Westernized countries, with higher prevalence of asthma, rhinoconjunctivitis and eczema, tend over time to acquire the rates of the local populations. However, most of this evidence has come from single-country studies with considerable differences in sampling methods and disease detection. Enter ISAAC—The International Study of Asthma and Allergies in Childhood—with data for over half a million children and adolescents from up to 111 centres in 48 countries. Analyses of ISAAC Phase Three data confirm existing evidence of a protective effect of migration from poor, low-prevalence countries to affluent, high-prevalence countries, that rapidly decreases with increasing time in the host country—findings that underline the importance of the environment over genetic factors in determining the prevalence of asthma, rhinoconjunctivitis and eczema.21

Operation Ranch Hand was a US-led and mainly US-operated military exercise during the Vietnam War. Inspired by the British use of herbicides during the Malayan Emergency in the 1950s, Ranch Hand involved spraying an estimated 77 million litres of herbicides over approximately 3.6 million acres in South Vietnam. Several herbicides were used, but Agent Orange was used the most extensively.22 Agent Orange contains several known carcinogenic dioxin impurities, including the most toxic form of dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin, or TCDD). The herbicides, procured from a number of companies, among them Dow Chemical Company and Monsanto,23 were used to clear foliage and deprive the population of food. Operation Ranch Hand began in 1962 and was terminated in 1971.24

From 1964 to 1973, South Korea sent around 320 000 troops to Vietnam, more than any other US ally. The study by Sang-Wook Yi and colleagues in this issue of the IJE examined the associations between Agent Orange/TCDD exposure and the risk of death in 180 000 of these Korean Vietnam veterans who survived the war and were still alive and traceable in 1992. Of these, nearly 18 000 died between 1992 and 2005. Mortality from all causes was elevated by exposure to Agent Orange/TCDD: deaths due to all cancers, several site-specific cancers and chronic myeloid leukaemia were positively associated with Agent Orange/TCDD exposure, as were deaths from angina pectoris, chronic obstructive pulmonary diseases and liver disease. The authors conclude that their study provides evidence suggesting that exposure to Agent Orange/TCDD several decades earlier may account for this increased mortality.25

The effects of exposure to Agent Orange/TCDD on US personnel and their allies serving in Vietnam have been the subject of numerous studies and reports.22,24,26 In 1991, Congress passed the Agent Orange Act. Among other provisions, this Act directed the Secretary of Veterans Affairs to request the Institute of Medicine to undertake a comprehensive evaluation of the health effects of exposure to Agent Orange/TCDD and other herbicides used in Vietnam. The first Veterans and Agent Orange (VAO) report was published in 1994 and the ninth, congressionally
mandated, biennial update was published in December last year. As in previous VAO updates, the 2012 report presents the scientific committee’s evaluation of peer-reviewed scientific papers published October 2010–September 2012, concerning associations between health outcomes and exposure to TCDD and other chemicals in the herbicides used in Vietnam. Findings from these papers, which include studies of people exposed in occupational and environmental settings as well as Vietnam veterans, are integrated with the evidence established at the time of the previous update and summarized. Outcomes for which there is sufficient evidence of an association or suggestive or limited evidence of an association are shown in Box 1.

**Box 1 Reproduced from Table S-1, Summary of Ninth Biennial Update of Findings on Vietnam-Veterans, Occupational, and Environmental Studies Regarding Scientifically Relevant Associations Between Exposure to Herbicides and Specific Health Outcomes**

**Sufficient evidence of an association**
Epidemiologic evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between exposure to herbicides and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free of bias and confounding show an association that is consistent in magnitude and direction, there could be sufficient evidence of an association. There is sufficient evidence of an association between exposure to the chemicals of interest and the following health outcomes:

- Soft-tissue sarcoma (including heart)
- Non-Hodgkin lymphoma
- Chronic lymphocytic leukemia (including hairy cell leukemia and other chronic B-cell leukemias)
- Hodgkin lymphoma
- Chloracne

**Limited or suggestive evidence of an association**
Epidemiologic evidence suggests an association between exposure to herbicides and the outcome, but a firm conclusion is limited because chance, bias, and confounding could not be ruled out with confidence. For example, a well-conducted study with strong findings in accord with less compelling results from studies of populations with similar exposures could constitute such evidence. There is limited or suggestive evidence of an association between exposure to the chemicals of interest and the following health outcomes:

- Laryngeal cancer
- Cancer of the lung, bronchus, or trachea
- Prostate cancer
- Multiple myeloma
- AL amyloidosis
- Early-onset peripheral neuropathy
- Parkinson disease
- Porphyria cutanea tarda
- Hypertension
- Ischemic heart disease
- Stroke (category change from Update 2010)
- Type 2 diabetes (mellitus)
- Spina bifida in offspring of exposed people

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*This table is the product of the Committee for Update 2010; the current committee has decided to add ‘scientifically relevant’ before ‘association’ in its own work product to emphasize the scientific nature of the VAO task and procedures without implying any change in the present committee’s criteria from those used in previous updates.

†Herbicides indicates the following chemicals of interest: 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and its contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin), cacodylic acid, and picloram. The evidence regarding association was drawn from occupational, environmental, and veteran studies in which people were exposed to the herbicides used in Vietnam, to their components, or to their contaminants.

*Evidence for an association is strengthened by experimental data supporting biologic plausibility, but its absence would not detract from the epidemiologic evidence.

*The committee notes the consistency of these findings with the biologic understanding of the clonal derivation of lymphohematopoietic cancers that is the basis of the World Health Organization classification system.

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The tenth and final VAO update was due to commence in October of this year. Published online on 2 September, the findings of Yi and colleagues will doubtless be reviewed by the committee and, being such a large study, will add to evidence of adverse effects on a number of the outcomes listed in Box 1. One of the advantages of the Korean Veterans study is that its findings are based on a comparison between veterans with low and high exposure to Agent Orange/TCDD. Whereas this is an improvement over studies which have used control veterans not exposed to herbicide or members of the general population, the level of actual exposure to Agent Orange/TCDD is a highly contested topic.27

Following a recommendation in the original VAO report28 that a historical exposure-reconstruction approach suitable for epidemiological studies be developed, a project ‘Characterizing Exposure of Veterans to Agent Orange and Other Herbicides in Vietnam’ was set up by a team of researchers at Columbia University’s Mailman School of Public Health. The Columbia team integrated various sources of information on spray activities and locations of military units, to generate individualized estimates of exposure.29 An Institute of Medicine report in 2008 examined the feasibility of using the Agent Orange Reconstruction Model developed by Columbia University and concluded that, despite shortcomings, the model should be used to conduct epidemiological studies of ground troops.27 Yi and colleagues determined the dates and location of each of the units in which the Korean veterans served. This information was sent to Stellman’s team who constructed unit-level exposure opportunity index scores by calendar day.25 However, the VAO for 2012 reported that ‘a pair of industry-sponsored papers’ had challenged the Stellman model and proposed an alternative that predicts a much smaller area under the spray path and Agent Orange/TCDD concentrations lower by several orders of magnitude than Stellman’s exposure opportunity index estimates for the same set of sample flight paths.27

Problems of exposure ascertainment certainly hamper definitive conclusions ascribing morbidity and mortality in veterans to Agent Orange/TCDD and, of course, are useful to those potentially in line to pay compensation claims. A statement on the Dow website distances the company to those potentially in line to pay compensation claims. A statement at the end of the paper reports complete independence from the sponsors Dow and Monsanto.24

Certainly the toxicity of TCDD is not in doubt. It was used to poison the Ukrainian president Victor Yushchenko in 2004,3 and a non-industry-sponsored meta-analysis of 22 studies published in this journal provided evidence that parental exposure to Agent Orange/TCDD appears to be associated with an increased risk of birth defects.35

**References**
