MIXED BAG

Air pollution and heart disease in women

The association between air pollution and death and hospitalisation due to cardiovascular disease is known. What we don't know is the magnitude of these effects, the mechanism and whether or not the relationship is dose dependent – does short-term exposure have the same effects as long-term exposure? Previous studies looking at long-term exposure (estimating exposure over years of follow-up) have only evaluated death certificates. What was found was that the increase in mortality associated with long-term exposure to air pollution is larger than that seen in studies of short-term exposure, and long-term effects on death rates serve as the current basis for fiercely challenged environmental regulations in the USA.

The authors of this study, recently published in the *New England Journal of Medicine*, evaluated long-term exposure to air pollution and the incidence of cardiovascular disease in the Women's Health Initiative (WHI) Observational Study, a prospective cohort study with medical-record review and classification procedures designed to document specific first cardiovascular events. They also examined how between-city and within-city gradients of exposure to particulate matter of less than 2.5 µm in aerodynamic diameter ($PM_{2.5}$) are associated with first cardiovascular events.

The WHI enrolled postmenopausal women between the ages of 50 and 79 years in the study from 1994 to 1998. The authors used data on the monitoring of air pollution from the Environmental Protection Agency's Aerometric Information Retrieval System with the use of AirData. Such data are recorded for $PM_{2.5}$ and particulate matter of less than 10 µm in aerodynamic diameter (PM_{10}), sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone. They selected monitors on the basis of monitoring objectives and scale to represent ambient community-scale exposure and excluded those with data available from less than 50% of intended samples. The long-term average $PM_{2.5}$ concentration was the exposure of interest, and the annual average concentration in the year 2000 was the primary exposure measure.

Rather than looking at death certificates, this study looked at the first cardiovascular event: any of myocardial infarction, coronary revascularisation, stroke and death from either coronary heart disease or cerebrovascular disease. A total of 1 816 women, out of 65 893 women included in the study, had one or more fatal or nonfatal cardiovascular events, as confirmed by a review of medical records, including death from coronary heart disease or cerebrovascular disease, coronary revascularisation, myocardial infarction, and stroke. In 2000, levels of $PM_{2.5}$ exposure varied from 3.4 to 28.3 µg per cubic meter. Each increase of 10 µg per cubic meter was associated with a 24% increase in the risk of a cardiovascular event and a 76% increase in the risk of death from cardiovascular disease. For cardiovascular events, the between-city effect appeared to be smaller than the within-city effect. The risk of cerebrovascular events was also associated with increased levels of $PM_{2.5}$.

The conclusion was that the incidence of cardiovascular disease and death among postmenopausal women is associated with long-term exposure to fine particulate air pollution. This study took place in the USA, admittedly not one of the greenest countries in the world. But if we consider the amount of fine particulate matter in the air of cities in the developing world, how much more cardiovascular disease must be present among older women in these countries.

Miller KA *et al*. *NEJM* 2007; 356: 447-458.

Erythropoietin and target haemoglobin concentrations

As someone interested in cycling I have often heard of erythropoietin (EPO) used to improve endurance performance among the world's elite cyclists – sometimes with untoward results, such as heart attack, stroke and even premature death. Now, a recent paper in *The Lancet* suggests that assiduous targeting of higher haemoglobin levels in anaemic patients with chronic kidney disease may also cause adverse events.

The authors did a meta-analysis of randomised controlled clinical trials, using trials that assessed the effects of targeting different haemoglobin concentration in patients with anaemia caused by chronic disease who were randomly assigned to treatment with recombinant EPO. They found 9 trials that enrolled 5 143 patients. There was a significantly higher risk of all-cause mortality and arteriovenous access thrombosis in the higher haemoglobin target group than in the lower haemoglobin target group. There was also a significantly higher risk of poorly controlled blood pressure in the higher haemoglobin group. The incidence of myocardial infarction was much the same in both groups.

The author's suggestion is that targeting higher haemoglobin concentrations when treating patients with anaemia caused by chronic kidney disease using EPO puts the patients at increased risk of death. Current guidelines do not include an upper limit for target haemoglobin concentration and they suggest that this should be considered in future recommendations. Cyclists and other endurance athletes should also beware.

Phrommintikul A *et al*. *Lancet* 2007; 369: 381-388.

Bridget Farham

IN MEMORIAM

Ariel Reyes

Professor Ariel Jorge Reyes y Garcia, a friend of academic medicine in South Africa, died in Montevideo, Uruguay in August 2006, shortly after his 63rd birthday. His involvement in original research at the University of Natal Medical School between 1979 and 1991 did much to bring that institution to the attention of colleagues in the Americas and the Latin countries of Europe.

Ariel Reyes was a product of the Uruguayan professional classes; cultured, a devout scientist, well-informed, widely read, competent in at least four European languages and at home in many great cities. Trained at the Universidad de la Republica, Montevideo, he spent his first postgraduate years in the Department of Physiology. He refined his vocational training in the Cardiology Department of Leeds, directed by the late Stanley Taylor, who considered Reyes to be his brightest research and clinical fellow. His best work was performed in cooperation with Fundación Procardias in Montevideo and during visits to the Department of Clinical and Experimental Pharmacology at the University of Natal, South Africa.

The perceived unimportance of South America to people in the Anglophone and central European countries meant that the value of his original contributions to medical science was not immediately recognised. During the last three decades Reyes published more than 200 papers and delivered innumerable lectures, many in collaboration with his friend Professor Perry Leary, initially in Natal and Montevideo and later in Ireland and Uruguay. He coordinated outstanding clinical research in hypertension and congestive heart failure in Germany and Italy with Guiseppe Crippa, and contributed to the theoretical and practical development of new drugs, including torasemide and nolomirole. His mastery of statistics, an uncommon endowment among clinical investigators, enabled him to participate in the design and analyses of the studies he coordinated or carried out personally.

Reyes was unafraid of criticism. A number of published papers first provoked heated debate but subsequently became incorporated in accepted therapeutic wisdom, usually with minimal reference to him and his collaborators. He was among the earliest investigators to postulate (and demonstrate) that ACE inhibitors could be effective in lowering 24-hour blood pressure when administered once daily, irrespective of plasma kinetics. He applied mathematical models to the urinary flows of water and solutes after the dosing of placebo or diuretics to healthy volunteers and identified rational modifications of diuretic use in patients. A mathematical model was also fitted to data from treated and untreated hypertensives, proving that whereas the rate at which a drug lowers blood pressure, over time, depends on the drug class and the dose given, the final effect over 10-12 weeks tends to be much the same. He and his colleagues proved the concept that sub-diuretic doses of common diuretics exist; these doses gradually reduce raised blood pressure over a period of weeks with little or no disruption of fluid or electrolyte balance. The absence of mathematical literacy among the medical profession meant that these proofs of clinical theories did not receive the acclaim they deserved. The scientific community is indebted to him, *inter alia*, for the changes he promoted in diuretic use, saving many hypertensive patients from the untoward consequences of electrolyte imbalances caused by unnecessary use of high diuretic doses.

Reyes was motivated by strong principles of scientific honesty and was not diplomatic in dealing with simpler individuals or with those who did not share his enthusiasms. Many of his ideas would remain incomprehensible to colleagues and to a pharmaceutical industry that failed to appreciate how much could be gained by employing his expertise during the early phases of drug development. The exception was his contribution to the development of torasemide. He remained an independent voice to the end, quite uncorrupted by financial inducements.

Reyes was an active member of numerous committees that organised international meetings in both the Americas and in Europe and a key figure in at least one South African congress. He also served on the editorial boards of various important English and Spanish journals. Ever present at international congresses, Reyes was not active as a lecturer, much preferring to question speakers from the chair or the floor and extracting full value from informal discussions in coffee houses that he would rapidly pollute with cigarette smoke.

Xenophobic by instinct and intensely proud of his own cultural roots, he befriended and respected anyone scientifically reliable within his chosen academic and research fields. Ariel Reyes could be a difficult person to walk beside; highly intelligent, complicated, lucid and amusing, a loyal friend, he was also demanding of his family, colleagues and, with fatal consequences, himself. He drove himself in pursuit of only the best academic and scientific standards, such that his personal life was less than ideal and his sudden death probably inevitable.

His provocative presence will be missed at many future gatherings of clinical pharmacologists and cardiologists. His contributions to science will be recognised in due course. His friends and family, who loved him unconditionally, will remember him with great affection always.

Perry Leary

Albert Coetzee

Professor AM (Albert) Coetzee is op 3 Oktober 2006 in die ouderdom van 85 jaar in Pretoria oorlede.

Sy studente en kollegas sal hom onthou as 'n veelsydige mens met 'n belangstellingsveld en 'n spektrum van betrokkenheid wat ver buite die geneeskunde uitgekring het.

Die feit dat hy, benewens sy geneeskundige kwalifikasies, ook 'n gegradueerde myningenieur was, het hom by uitstek geskik vir sy taak as professor van bedryfsgeneeskunde gemaak. Hy was 'n leermeester wat die fyn balans tussen teorie en praktyk tot 'n kuns bemeester het. Sy samestelling en aanbieding van die diplomakursus in bedryfsgeneeskunde het hiervan getuig. Om dit te kon bereik, het hy lektore en aanbieders uit 'n groot aantal verbandhoudende dissiplines betrek. Die praktiese deel van die kursus, aan die hand van besoeke aan nywerhede, was wyd en goed gekies. Alles tussen die diepste goudmyn en lugvaartgeneeskunde, het iemand eenkeer gesê. Dan bly dit 'n mens by dat professor Penalver, 'n Kubaanse boorling verbonde aan die Universiteit van Miami, aan ons gesê het dat dit 'n voorreg is om onder die leiding van so 'n man van wêreldformaat te kon staan.

Terwyl hy nog Direkteur van Mediese Dienste by Rand Mines was, 'n pos wat hy 15 jaar lank beklee het, was hy by baie ander aktiwiteite betrokke. Die ouer garde sal die reeks praatjies onthou wat oor die radio uitgesaai is. Hy was ook vir baie jare aktief betrokke by die SA Rooikruisvereniging.

Ek het hom leer ken as offisier by 5 Veldambulans, SA Geneeskundige Diens, waar hy as vrywilliger diens gedoen en later met die rang van majoor uitgetree het. Hy was ook baie aktief betrokke by die Voortrekkers en was kommandant van die Linden Kommando.

Sy droë humorsin verdien vermelding. Ek het eenkeer vir hom gesê dat dit half ongewoon klink dat hy die AM Coetzee gedenklesing aanbied. Nee, sê hy, toe die jaarlikse lesing ingestel is, het hulle gedink hy gaan nie nog 'n jaar lewe nie, en kyk nou net.

Met 'n laaste taptoe salueer ons een van die stoere grondleggers van die beroepsgeneeskunde in Suid-Afrika.

Ben Botha
Brakpan

Nicolaas van der Westhuizen (22/5/1917 – 26/9/2006)

Oom Nic, soos ons hom almal geken het, is op 26 September 2006 in Pretoria aan hartversaking oorlede. Hy was 89 jaar oud.

Vir 30 jaar was hy my beste vriend en mentor. As psigiater het hy my bipolêre steurnis wat my toe lamgelê het, gou in beheer gebring en al die jare so gehou. Daarvoor kan ek hom nie genoeg bedank nie. Hy was 'n meester in sy vak.

Oom Nic is op 'n plaas in die Koster distrik gebore en het in Rustenburg skoolgegaan. Hy het aan die Potchefstroomse Universiteit vir CHO onderwys bestudeer en 'n paar jaar skoolgehou voordat hy sy mediese studies begin het. Op mediese skool was hy 'n paar jaar ouer as sy medestudente, en het as 'meester' bekend geword.

Hy en sy eerste vrou, Myda, het vyf kinders gehad: Mariette (onderwyseres), Johann (ortopeed), Lourika (oogarts), Rosalie (dieetkundige, met gastehuise) en Henrico (onderwyser en boer). Na Myda se dood is Nic met dr. Stella Salmond getroud, en hulle was meer as 30 jaar saam.

Nic het by verskeie psigiatriese inrigtings gewerk en was jare lank in bevel van die inrigting by Sterkfontein. Hy was 'n Christen en altyd nederig en geduldig, en baie gasvry – 'n mens was altyd welkom in hul huis.

Nic is in die Sterkfontein begraafplaas te Krugersdorp begrawe.

Frans de Wet