Response to ‘Downloadable computer models for maintenance but not acute renal replacement therapy’

We are grateful to Drs Marshall and Golper for pointing out that when flows are low, dialyzers may not achieve the clearance rates predicted from values for $K_{dA}$ that are derived from clearances measured at higher flows. We should have noted in addition that clearances in vivo are often lower than those predicted from manufacturers’ $K_{dA}$ values, which are usually derived from clearance experiments performed with saline solutions. An even greater problem is that $K_{dA}$ values are usually available only for urea, creatinine, and vitamin B$_{12}$, and must be guessed at for other solutes of interest. We disagree somewhat with Drs Marshall and Golper about the application of the models to acute renal failure. We should emphasize that it is only the downloadable format, and not the theoretical content, of our models that is new. Like other theoretical models, they can predict plasma solute concentrations only when solute production rates, solute distribution volumes, and residual renal function are specified, and these latter parameters are both variable and hard to estimate in acutely ill patients. But we think that the models can still be useful in helping nephrologists to think about solutes other than urea. An example may be provided by the description of sustained low-efficiency dialysis with $Q_B$ of 200 ml/min and $Q_D$ of 100 ml/min to which Marshall and Golper refer. If urea is the only solute considered, the predicted clearance is not much different for $Q_B$ of 200 ml/min and $Q_D$ of 100 ml/min as compared to $Q_B$ of 100 ml/min and $Q_D$ of 200 ml/min. But the models predict that the clearance of solutes, which bind to plasma proteins, will be higher using $Q_B$ of 100 ml/min and $Q_D$ of 200 ml/min. We think it is wrong to assume that all uremic toxins behave like urea, and that modeling the effect of renal replacement therapies on other classes of solutes may thus have some value.


T Meyer$^1$ and T Hostetter$^2$

$^1$Department of Medicine, Stanford University and Palo Alto VA Medical Center, Stanford, California, USA and $^2$Department of Medicine, Albert Einstein College of Medicine, Bronx, New York, USA

Correspondence: T Meyer, Department of Medicine, Stanford University and Palo Alto VA Medical Center, 38001 Viruuda Ave, Bldg 100, Room E2-100, Palo Alto, California 94304, USA. E-mail: twmeyer@stanford.edu

Hardy–Weinberg equilibrium and control subjects

We are grateful to Drs Marshall and Golper for pointing out that when flows are low, dialyzers may not achieve the clearance rates predicted from values for $K_{dA}$ that are derived from clearances measured at higher flows. We should have noted in addition that clearances in vivo are often lower than those predicted from manufacturers’ $K_{dA}$ values, which are usually derived from clearance experiments performed with saline solutions. An even greater problem is that $K_{dA}$ values are usually available only for urea, creatinine, and vitamin B$_{12}$, and must be guessed at for other solutes of interest. We disagree somewhat with Drs Marshall and Golper about the application of the models to acute renal failure. We should emphasize that it is only the downloadable format, and not the theoretical content, of our models that is new. Like other theoretical models, they can predict plasma solute concentrations only when solute production rates, solute distribution volumes, and residual renal function are specified, and these latter parameters are both variable and hard to estimate in acutely ill patients. But we think that the models can still be useful in helping nephrologists to think about solutes other than urea. An example may be provided by the description of sustained low-efficiency dialysis with $Q_B$ of 200 ml/min and $Q_D$ of 100 ml/min to which Marshall and Golper refer. If urea is the only solute considered, the predicted clearance is not much different for $Q_B$ of 200 ml/min and $Q_D$ of 100 ml/min as compared to $Q_B$ of 100 ml/min and $Q_D$ of 200 ml/min. But the models predict that the clearance of solutes, which bind to plasma proteins, will be higher using $Q_B$ of 100 ml/min and $Q_D$ of 200 ml/min. We think it is wrong to assume that all uremic toxins behave like urea, and that modeling the effect of renal replacement therapies on other classes of solutes may thus have some value.


MR Marshall and TA Golper

1Department of Renal Medicine, Middlemore Hospital, Auckland, New Zealand and 2Vanderbilt University Medical Center, Medical Specialties Patient Care Center, Nashville, Tennessee, USA

Correspondence: MR Marshall, Department of Renal Medicine, Middlemore Hospital, Auckland, New Zealand. E-mail: mrmmarshall@middlemore.co.nz

Hardy–Weinberg equilibrium and control subjects

To the Editor: Consider a gene locus with two alleles, ‘A’ and ‘a’. The frequency of allele ‘A’ will be designated by $p$ and that of allele ‘a’ by $q$. Hardy and Weinberg showed that in a very large population with random mating, the frequencies of AA, Aa, and aa genotypes are $p^2$, 2$pq$, and $q^2$, respectively. The
Hardy–Weinberg formulation also predicts that the allelic frequencies will remain stable from generation to generation, provided that there is no mutation, no migration, and no natural selection in a very large population with random mating. If the evolutionary pressures are active and/or when the mating is not random, we can observe a significant deviation from the expected frequencies of the genotypes.

I read the article of Lin et al.1 with great interest and I would like to make a few comments about it. The authors determined a genetic polymorphism in the promoter region of heme oxygenase-1 gene and then investigated its association with arteriovenous fistula failure in Chinese hemodialysis patients in Taiwan. They also included 286 individuals without renal disease as control group. A dinucleotide repeat (GT) of different length was identified in the proximal promoter region of the human heme oxygenase-1 gene. The authors assigned those with GT repeats $\geq 30$ as allele class L (long) and those with GT repeats $< 30$ as allele class S (short).

Based on Table 2 of the article of Lin et al.,1 61, 163, and 62 persons showed S/S, L/S, and L/L genotypes, respectively. There is significant deviation from Hardy–Weinberg equilibrium ($\chi^2 = 5.595, df = 1, P = 0.025$).

Unfortunately, the authors did not mention why their control group is not on Hardy–Weinberg equilibrium. Is there any problem for selecting the control subjects? The observed frequency for the heterozygote genotype was 56.9%, whereas the expected frequency of the genotype was 49.9%.

On the other hand, both homoyzgote genotypes were decreased in the control group compared to expected values. Therefore, it is possible that the control subjects were chosen from at least two different gene pools (or different populations). What can we say about the patients? If they belong to different gene pools, is there any difference(s) between these populations for the prevalence of coronary artery disease, cardiovascular disease, and arteriovenous fistula failure? Finally, it seems that the reliability of the results of Lin et al.1 dramatically decreased, and therefore their findings must be interpreted with caution.

Response to ‘Hardy–Weinberg equilibrium and control subjects’


The authors thank Saadat1 for raising an essential issue regarding Hardy–Weinberg equilibrium in carrying out case-control association studies. In our paper, the main theme was to analyze the association between HO-1 repeat polymorphisms and arteriovenous fistula patency in patients underwent hemodialysis. Thus, the comparisons were mostly based on differences of genotypes between the two case groups, that is those with and without fistula failure. Hardy–Weinberg equilibrium was not violated in the two case groups; therefore, the tests that we performed were valid and so did the conclusions.

We were aware of the deviation of Hardy–Weinberg equilibrium for the control group; therefore, the test of association between Huntington’s disease patients and controls was carried out by Armitage’s trend test (a valid test even in Hardy–Weinberg disequilibrium), which was not mentioned in our paper. To clarify further, we now add ‘using Armitage’s trend test’ in the footnote of Table 2 after ‘* signifies the $P$-value for the comparison between controls and Huntington’s disease patients’.

Regarding the variation among populations, we did genotype three informative SNP markers for Chinese subpopulations, rs727258, rs108996795, and rs10506294, to rule out population stratification.2 The results supported no difference between control and the two case groups (data not shown).


C-C Lin1,2,3, CS-J Fann4,5 and M-Y Chung5,6

1Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, Republic of China; 2School of Medicine, National Yang-Ming University, Taipei, Taiwan, Republic of China; 3Division of Nephrology, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China; 4Division of Epidemiology and Genetics, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan, Republic of China; 5Institute of Genome Sciences, National Yang-Ming University, Taipei, Taiwan, Republic of China and 6Department of Medical Research, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China

Correspondence: M-Y Chung, Department of Medical Research, Veterans General Hospital-Taipei, No. 201, Sec. 2, Shih-Pai Road, Taipei, Taiwan 112, Republic of China. E-mail: mychung@vghtpe.gov.tw

Ultrasonography and graft patency


To the Editor: Robbin et al.1 have recently published an interesting randomized study assessing the impact of ultrasound surveillance on arteriovenous graft outcomes. This study failed to prolong graft patency by means of screening ultrasonography. This finding is in contradiction to our randomized study,2 published a couple of months earlier, where adding of ultrasound to clinical monitoring was associated with significantly longer graft patency. A post hoc analysis by Dossabhoy et al.3 supported our data.