requires us to select the right tool or tools for each particular job. Thus, much as I would choose a hammer to drive a nail into place, I would include the use of contact isolation in the management of a patient with infectious diarrhea or a draining wound (hardly "exceptional cases").

It is said that to a person with a hammer, everything looks like a nail, and perhaps this is even more true of someone who consults for a hammer company. When 2 experts in the field of health care epidemiology repeatedly call for "every health care facility" to implement a program of active detection and isolation, they rightfully attract our attention. When one of these experts discloses potential conflicts of interest that include a relationship with a company that markets a diagnostic test for MRSA, we must view these calls with caution.

A hammer, and even a wrench, might drive a screw into a piece of board. In the case of a screw, though, a better tool is available. My paper was intended to help hospitals consider conditions in which isolation might be the most appropriate tool for preventing health care–associated infections. A similar approach to the rest of the toolbox seems warranted.

Acknowledgments

Potential conflicts of interest. K.B.K.: no conflicts.

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Clinical Infectious Diseases 2009; 49:988–9

1058-4838/2009/4906-0028$15.00
DOI: 10.1086/605537

From Plasma BK Viral Load to Allograft Damage: Rule of Thumb for Estimating the Intrarenal Cytopathic Wear

To the Editor—The BK virus, which is a member of the polyomavirus family, is the etiologic agent of polyomavirus-associated nephropathy, a disease affecting ≤10% of kidney transplant recipients with irreversible loss of allograft function. With the increased potency of new immunosuppressive drugs, polyomavirus-associated nephropathy has become an escalating threat [1]. Under transplant immunosuppression, lytic replication of the BK virus in kidney tubular epithelial cells drives the course of polyomavirus-associated nephropathy [2–4]. Removal of the kidney allograft is associated with vanishing BK viremia, usually within 1–2 weeks [3, 5].

Here we delineate how to estimate the BK virus–mediated intrarenal cytopathic wear directly from data on quantitative plasma BK viral load. Our rule of thumb proposes that a BK viral load of 1000 copies/mL corresponds to 1 lysed cell per day. Hence, a BK viral load of 50,000 copies/mL would result in a cytopathic wear of $\sim 1.25 \times 10^5$ cells per individual per day (90% confidence interval, $0.31–5 \times 10^5$ cells per individual per day) (figure 1*A*).

The in vivo half-life of the BK virus after removal of the source of viral replication (ie, after nephrectomy) has been estimated to be 1–2 h [3]. Thus, during a 24-h period, a given viral load decreases 2^{12}–2^{24}-fold (figure 1*B*). To maintain a dynamic equilibrium state for 24 h, ongoing replacement of plasma virus is required, with a replacement rate of ~10 per day (half-life, 1.5 h) [3]. Hence, the daily viral turnover with replacement is ~10 times a detected viral load (≈1000%). During phases of viral expansion or contraction, a (stepwise) integration over the viral-load changes would be required (figure 1*C*). Data from patients who show histological evidence of polyomavirus-associated nephropathy indicate in situ a mean burst size of ~10,000 virions per infected host cell (range, 3–44,000 virions per infected host cell)—in line with recent in vitro experiments yielding a somewhat higher intracellular BK viral DNA load per cell [6–9]. Division of the total viral turnover by the burst size yields the number of host cells liberating their viral progeny into plasma; in this case, a BK viral load of 1000 copies/mL would correspond to 1 cell per day. Hence, plasma viral loads—scaled to whole-body levels—serve as a rough approximation of the daily intrarenal cytopathic wear associated with BK virus replication. For a packed cell volume (hematocrit) of 0.5, the formula further simplifies to $X \times 2.5 = Y$, where X denotes the detected plasma BK viral load in copies/mL and Y denotes the daily cytopathic wear per individual (figure 1*A*; see "one-step calculator"). If the plasma BK viral loads represented 1% of the virus produced in the allograft, then the true cytopathic wear would be 100 times higher. Other percentages change this estimate proportionately. Note that, because cells infected with the BK virus live on average 2–3 days before liberating their viral progeny [4, 8, 9], at any time, the infected cells exceed the lysed cells by a factor of 2–3. The simple rule-of-thumb approximation breaks down when viral fluxes between distinct replication sites come into play. In such complex systems, mathematical modeling still allows one to disentangle the respective cytopathic contributions [10].

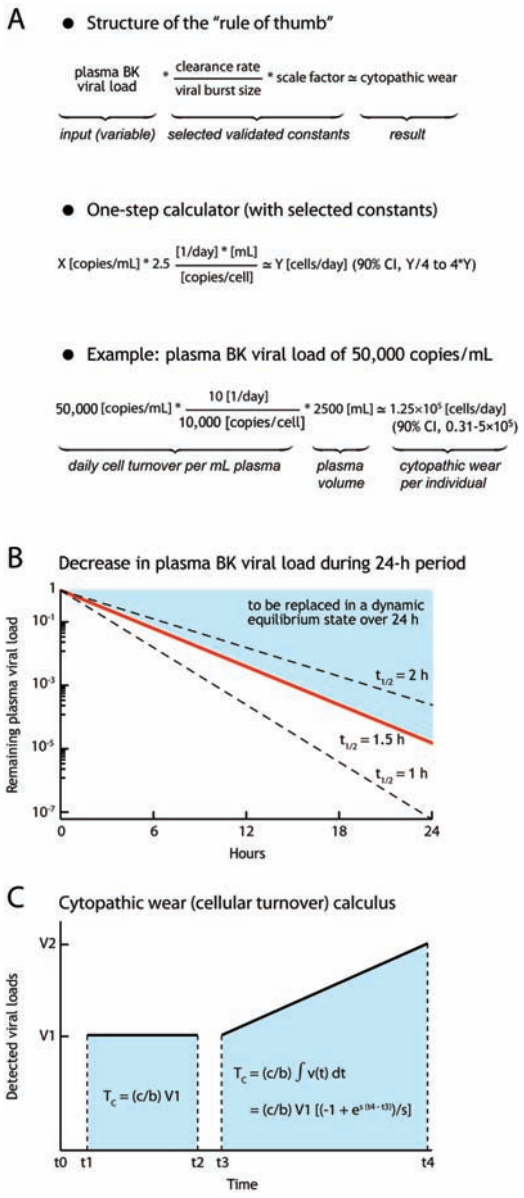

Figure 1. *A,* Structure of the rule of thumb, one-step calculator, and numerical example. The input BK viral load is 50,000 copies/mL. The selected constants and/or parameter values are as follows: c, 10 per day (half-life, ~1.5 h); b, 10,000 progeny viruses per host cell; blood volume, 5 L, packed cell volume (hematocrit), 0.5. The BK viral loads, the clearance (replacement) rates, and the burst sizes (all derived from the use of polymerase chain reaction) each have an error of ⩽2, which yields a 90% probability that our estimate deviates ⩽4-fold and a 70% probability that it deviates ⩽2-fold from the true value. Note that replacing our selected constants by other (patient-specific) values affects the result in a linear manner; however, the deviation probabilities do not change. *B,* Viral decay during a 24-h period plotted on a log scale. The red line represents the decay curve for a viral half-life of 1.5 h; the black dashed lines represent decay curves for viral half-lives of 1 and 2 h, respectively. The light blue area represents the viral load to be replaced during a 24-h period, to maintain a dynamic equilibrium state. *C,* Cytopathic wear, where T_c denotes cellular turnover in a dynamic equilibrium state *(left)* or during viral expansion *(right).* The correction term for expanding (or contracting) viral loads is given in the squared bracket. Its derivation requires some calculus, where c is the viral replacement rate [1/day]; b is the viral burst size per host cell [viruses/cell]; V1 and V2 are the detected viral loads [copies/mL]; t1 and t2 are the sampling times [days]; and s is the slope of viral load change ($s = [\ln(V2) - \ln(V1)]/(t2 - t1)$).

Acknowledgments

Potential conflicts of interest. G.A.F. and H.H.H.: no conflicts.

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Clinical Infectious Diseases 2009; 49:989–90

1058-4838/2009/4906-0029$15.00
DOI: 10.1086/605538