## Can TB Transmission in Community Congregate Settings be Controlled Environmentally? - like Cholera from Snow's Contaminated Well

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The extremely thoughtful article by Yates and colleagues on the need for greater environmental control of TB in the community deserves praise and comment. First, the idea is not new, as suggested by their paragraph entitled, "Back to the Future". Not long after Wells and Riley proposed (and much later proved) droplet nuclei transmission for TB and other infections, public health authorities envisioned broad environmental control interventions analogous to public water purification, or historically, removing the pump handle for a cholera contaminated public well to effectively control transmission at the source for that water-borne disease. Focused on temperate climates in developed countries, early public health visionaries considered a variety of air disinfection strategies, from mechanical ventilation to glycol vapor fog, and especially upper room germicidal UV because it was relatively inexpensive and highly effective.

A lot has changed since Wells' 1955 landmark monograph on Airborne Contagion and Air Hygiene, and Riley's 1961 shorter monograph contemporary with his experimental ward human-to-guinea pig TB transmission studies. However, the need for air disinfection seemed less important with the advent of vaccines for the epidemic respiratory viruses like measles and smallpox, and the discovery of antibiotics for tuberculosis. Such infections were to be a thing of the past. It was the 1985-92 US and Western Europe resurgence of TB, often associated with HIV and drug resistance, that heralded the coming global MDR-TB/HIV crisis – and the renewed need for effective environmental control measures in congregate settings. Without firm evidence CDC and WHO set ventilation goals, emphasizing natural ventilation based largely on optimistic estimates of efficacy based on CO2 clearance studies. Upper room germicidal UV (GUV) air disinfection, although known to be effective for decades, was thought to be less well understood and lacking evidence for safety and efficacy. Room air cleaners were widely sold in the US, but most devices moved far too little air to be useful. But as TB in the US returned to pre-resurgent low levels - and continues to decline slowly to record low levels, the real need for transmission control strategies has shifted to the global stage – not only in relatively warm climates in Africa and Asia – but also in cold climates like Eastern Europe where drug resistance is rampant and where natural ventilation has very little practical role.

There are few epidemiological studies of environmental control of airborne infections. One of the most convincing was a controlled study reducing measles transmission with upper room GUV in school classrooms in the Philadelphia suburbs, conducted by Wells and colleagues in the 1930s. But while this important study unequivocally demonstrated efficacy in the wealthy Philadelphia suburbs where children were driven to school, the same intervention failed to be effective in schools in a rural upstate New York setting where children were transported in school buses, or in schools in urban London where children returned to crowded tenements. The message was an important one. Even powerfully effective interventions like upper room GUV (properly applied, see below) may not impact transmission unless applied in the most important sites of transmission. Unlike Snow's well where removing the handle stopped a cholera epidemic, the air we breathe comes from many different sources where contamination from many different unsuspected, untreated TB cases is possible. The challenge that Yates and colleagues revive is - can we now better identify the key sites of transmission using current epidemiological tools, and is it practical to apply effective environmental controls to impact the epidemic? They wisely suggest this approach together with conventional surveillance and treatment approaches (DOTS) – and with enhanced approaches such as active case finding and rapid effective treatment in the community, or specifically in congregate settings (F\_A\_S\_T).

What new developments might make environmental controls more important and effective now than in the past when? Molecular epidemiology and social network science combined with old fashioned shoe leather contact investigations has improved the accuracy of determining sites of transmission in the community, although transmission patterns remains heavily skewed by super-spreaders and chance, making risk prediction an imperfect science at best. Social determinants of Mtb transmission and disease are also now better understood, contributing to better targeting of higher risk populations and sites. Still, unlike Snow's well, TB remains a disease with far too many potential sources for complete control by environmental means alone. As noted, identifying unsuspected sources of transmission – both unsuspected cases and unsuspected drug resistance – and promptly beginning effective treatment remains as important as was the correct identification of the unsuspected cholera-tainted well. Rapid diagnostics has helped greatly with identifying sources, as has the recognition of the importance of active case finding in selected settings.

Finally, the available interventions, although not fundamentally expanded in number, are now better understood in terms of their technical application. That understanding applies as well to interventions unlikely to work at all, or unlikely to consistently work well. Natural ventilation, although the most ubiquitous environmental intervention, and still underused, has also been oversold as the answer to the environmental control of Mtb. Unreliable climatic conditions, closed windows at night, and poor air movement in interior spaces are among many reasons why natural ventilation cannot alone address the environmental control of airborne infections, especially in cold climates – but also in warm climates as split system cooling is introduced to prevent heat-related deaths, windows are closed. Extraction fans are also ubiquitous and, properly applied, can help assure directional airflow and some ventilation in some poorly ventilated spaces. But a simple smoke stick can easily demonstrate that contaminated air just a meter or so away from the fan is unlikely to move toward the fan, drifting up and dispersing into room air. Room air cleaners of countless configurations continue to be designed by engineers and sold to unwary hospital administrators, but we know now that their relatively low clean air delivery rates, minus short circuiting of just filtered air back into these devices, greatly limits their utility in all but the smallest of unventilated rooms. Upper room GUV air disinfection, with air mixing, continues to have its skeptics and navsavers, but in the view of this author, remains the environmental intervention with the greatest potential to impact Mtb transmission. It is also the most cost-effective intervention after natural ventilation. We now know how to safely apply effective GUV extremely well and we understand the barriers and how to overcome them. The barriers are: 1) lack of capital funds for the purchase and installation; 2) lack of expertise to plan upper room GUV; 3) lack of low-cost, high quality GUV fixtures; 4) lack of UV laboratories to measure total fixture UV output for dosing purpose; 5) lack of maintenance capacity in most hospitals, clinics, and other congregate settings; and 6) lack of reliable electricity in some settings.

Most of these barriers are addressed by a proposed new model of comprehensive sustainable commercial GUV services where a local vendor to hospitals provides expertise to plan, install, commission, and maintain quality GUV fixtures of known UV output for a profitable but fair leasing fee, with oversight by a local health agency. Not yet established anywhere in the world, efforts are underway to pilot such programs simultaneously in several high burden settings. Until demand justifies the manufacture of high quality locally made fixtures, pilot programs can begin by assembling high-quality fixtures from components manufactured abroad. Current upper room GUV fixtures must have output fully characterized in a qualified lighting laboratory (by the manufacturer) in order to apply recently published dosing guidelines. Perhaps the main motivation for the design-lease-maintain model is the maintenance component – the single greatest challenge for any technology that is introduced into resource-limited settings. Whether this model will work well enough to address the barriers to global implementation of upper room GUV remains to be seen, but it has the potential.

On the horizon are low-current LED GUV fixtures that will have the advantages of long lamp life and the ability to run off of batteries and solar power, addressing both power outages and limited access to electricity. Another novel approach to upper room GUV in buildings with enough ceiling height is "eggcrate ceiling UV" where unlouvered fixtures are combined with an eggcrate drop ceiling to achieve much greater efficiency while maintaining safety in the lower room.

In summary, Yates and colleagues have refocused our attention on the potential for environmental controls to reduce nosocomial spread of TB – ideally in conjunction with institutionally based rapid case finding and effective treatment (FAST). While not a new idea, it may be one that deserves greater attention if the global MDR TB epidemic is going to be controlled.