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Editorial

Trachoma: Time to Talk Eradication

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Trachoma was once the leading cause of blindness, endemic in nearly every country of the world.[1] As recently as the 1990s, trachoma still ranked second only to cataract as a cause of blindness.[2] Two decades ago, the World Health Organization (WHO) initiated a program to control the disease by 2020.[3] Although that goal will not be met on time, recent developments suggest that even loftier goals could be possible in the near future. Global eradication of the strains of *Chlamydia* that cause trachoma can be achieved, and sooner than previously thought, if we step up interventions in the most affected areas.

Most trachoma programs follow a WHO strategy that aims for control, defined as bringing infection to a low enough level that resulting disease is not a public health concern.[4] Elimination indicates that infection, or at least transmission of infection, is brought to zero in a geographical area. Eradication implies elimination of infection worldwide—at least outside of the laboratory. Smallpox remains the only infectious disease of humans eradicated by a public health program. A number of other infectious diseases are now on the ropes, including Guinea worm, polio, and onchocerciasis (river blindness).[5–7] Trachoma has several characteristics that make eradication at least feasible. Humans are the only host. Antibiotics are effective against *Chlamydia*, and no antibiotic resistance to azithromycin has yet emerged. Perhaps most importantly, trachoma benefits from an enormous secular trend. Trachoma disappeared in many regions without the benefit of specific trachoma programs. Where monitored longitudinally without active intervention, trachoma seems to be disappearing. Many agree that trachoma eventually will disappear with or without a public health program, although in the latter case, perhaps not for decades.[8–13]

As infection is eliminated in more countries, the argument that eradication is impossible becomes more difficult to make.

The cornerstone of the WHO program is mass treatment with a single-dose of oral azithromycin. Azithromycin was shown to be effective in clearing ocular chlamydial infection from most individuals.[14,15] Three weekly mass drug administrations (MDAs) appeared to be as effective as 6 weeks of the then standard-of-care topical tetracycline.[16] Subsequent community-randomized trials confirmed efficacy of mass distribution with a single dose of azithromycin.[17,18] Mathematical models suggested that annual distribution eventually could eliminate infection in most communities worldwide, although some may require more frequent treatment.[19] The International Trachoma Initiative and Pfizer, Inc. (New York, NY), have donated nearly 1 billion doses of azithromycin to the cause. After 20 years of distributions, districts that remain endemic now can be divided into those where infection will disappear regardless of any future MDA, those where infection will disappear with continued annual MDA, and those where infection will not disappear without more intensive intervention. The vast majority of endemic districts now fall into the first 2 categories.

The WHO relies on the clinical signs of trachoma to declare that a district has obtained control.[20] Specifically, control requires reducing the prevalence of follicular trachoma in the upper conjunctiva (TF) to be less than 5% in children. But TF can linger long after infection has been cleared. Thus, the community-level prevalence of TF is a lagging indicator.[21] In communities with a low prevalence of TF, infection often is impossible to find even with polymerase chain reaction analysis. Moreover, any association between TF and actual infection decreases after MDA.[22] Previously endemic countries, such as Nepal, Mexico, Ghana, Uganda, and the Gambia, recently performed population-based surveys as part of their dossiers to declare trachoma control. In each, polymerase chain reaction–determined prevalence of chlamydia in children was less than the false-positive rate of the test.[2–4] Ironically, by the time a country has been certified as controlled, elimination already may have occurred.

What about districts where more intensive intervention will be required? Approximately 30 districts in the Amhara region of Ethiopia remain far above control targets after a decade of MDA.[23] Perhaps an equal number of communities outside of Amhara will prove similar. Circumstantial evidence has suggested that water, sanitation, and hygiene measures could be complementary to MDA.[24] Unfortunately, no water, sanitation, and hygiene intervention has ever been shown to have any measurable effect on ocular chlamydial infection—not face washing, not latrine construction, and not water programs.[24,25] In fact, the only intervention ever proven to reduce infection more than annual MDA is more frequent MDA. Biannual distributions may reduce infection more rapidly than annual distributions and have completely eliminated infection from some of the most severely affected communities ever studied.[26–29] Quarterly distributions to children were proven superior to annual MDA in a community-randomized trial.[18] That study was designed as a proof of principle, to show that elimination of infection in children

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reduced infection in adults through an indirect, herd-like effect. At the time, no one realistically expected programs to distribute antibiotics quarterly to the thousands of endemic districts. But now, quarterly distributions to the few remaining problem districts may be more palatable than a second decade of annual MDA. Eliminating chlamydia as quickly as possible also may be the optimal way to address concerns about antimicrobial resistance and program fatigue.

Why not more enthusiasm for trachoma eradication? As infection is eliminated in more countries, the argument that eradication is impossible becomes more difficult to make. However, some argue that eradication is not necessary, that a low level of infection will never cause enough scarring to lead to blindness. That may well be true. But if infection is not eliminated in the problem areas, then the only proven way to maintain infection at a safe low level is continued MDA.[30] The enthusiasm for another decade or more of annual MDA may wane, and cessation of the program could result in resurgence of infection. Although infection eventually will disappear on its own, it is hard to blame WHO for not pushing a target of eradication. Failures to reach overly ambitious goals for malaria and leprosy are still remembered. But WHO and fellow stakeholders may now believe that they face a difficult decision: continue annual MDA for another decade and hope for the best, or intensify efforts in problem areas to accelerate the disappearance, and be the first to eradicate a bacterial disease? For us, that's an easy choice.

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