pertussis vaccines that induce antitoxin immunity and that are widely used in human populations argue against these predictions. The introduction of diphtheria toxoid vaccine at the beginning of the twentieth century led to a huge reduction in the number of people carrying the virulent form of this pathogen and to the persistence of non-virulent forms of the bacterium\(^1\). Diphtheria is caused by a toxin that is synthesized by Corynebacterium diphtheriae, which allows this bacterium to obtain nutrients when resources in the immediate vicinity are scarce. To produce the toxin, C. diphtheriae must carry a viral tox gene (tox\(^{1}\) strain). Toxin production therefore confers a competitive advantage — cases of frank diphtheria are more contagious than cases of asymptomatic infection.

However, toxin production also carries a metabolic cost. As the toxin is neutralized in people who are immunized with diphtheria toxoid, its production is a drain on the bacterium, which is therefore at a competitive disadvantage. Accordingly, diphtheria has vanished from areas with long-standing and thorough diphtheria-toxoid vaccination programmes, whereas the tox\(^{-}\) C. diphtheriae strain has persisted, a change that is attributable to the selective pressure exerted by the vaccine\(^6\).

A similar mechanism could explain the impact of the pertussis-vaccination programme implemented in Sweden with a vaccine containing only pertussis toxoid, which also induces antitoxin immunity. This vaccine was introduced in 1995 in 11 Swedish counties to vaccinate all children between 6 months and 14 years of age. Four years later, the result of this programme was a large reduction in hospitalized pertussis cases, not only in vaccinated but also in non-vaccinated children (that is, infants younger than 6 months old and children older than 14 years). This demonstrates once again that antitoxin immunity does affect pathogen transmission\(^6\).\(^6\)

Gandon et al. also argue that vaccines that counteract pathogen propagation may be less effective, as reduced transmission will elicit increased virulence. As we do not yet have an example of this type of vaccine for humans, we do not know whether this will be the case. This may be important for HIV vaccines\(^2\) as well as for malaria, but we suspect that the reduction in transmission of a pathogen that replicates on mucosal surfaces will outweigh any possible increases in endogenous virulence.

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**Figure 1** Evolutionarily stable toxin production, \(\tau^*\), plotted against antitoxin vaccine efficacy, \(r\), for different toxin-production costs, \(c\). Here it is assumed that all hosts are vaccinated, but similar results emerge for intermediate levels of vaccination coverage. The following transmission function was used: \(\beta(\alpha + (1 - r)\tau) = \beta_0(\alpha + (1 - r)\tau)^{\delta}\). Parameter values: \(\beta_0 = 1\), \(b_1 = 0.5\), \(\delta = 1\), \(\alpha = 0.2\).