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The sharpest tool in the shed: question-based clinical development of vaccines to address global health priorities

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The Sharpest Tool in the Shed
Question-Based Clinical Development of Vaccines
to Address Global Health Priorities

1. Implementing a question-based approach in clinical vaccine development reduces expenditure and accelerates development by prioritizing research questions based on both scientific and financial arguments. *This thesis*
2. A single-dose, late-arresting genetically attenuated malaria parasite has the potential to overcome critical limitations of current vaccines and as such holds significant promise as a next-generation malaria vaccine. *This thesis*
3. To overcome Shigella vaccine hyporesponsiveness in children living in high-endemic regions, Global North-South collaborations are essential to ensure that candidate vaccines are immunogenic across diverse epidemiological settings. *This thesis*
4. The low scale at which vaccine dose-optimization strategies were assessed during the COVID-19 pandemic reflects a structural failure in pandemic preparedness and highlights the need for public-sector mandates in vaccine development. *This thesis*
5. In future pandemics, researchers and clinicians involved in vaccine development should consider identifying the appropriate vaccine dosage that can save the most lives for a limited amount of antigen, rather than just a dosage that balances efficacy and reactogenicity for the individual person. *Cowling et al., Nature Medicine (2021)*
6. Vaccination into the dermal compartment addresses both the challenges of pandemic preparedness and vaccine hesitancy, and opens up avenues for novel vaccine formulation and dose-sparing strategies to enter the clinic. *Hettinga et al., Vaccines (2020)*
7. The biggest challenge for whole-sporozoite malaria vaccines is not direct venous inoculation, cryopreservation or the execution of mass vaccination campaigns. Rather, it is achieving the required vaccine efficacy of $\geq 90\%$ sterile protection in the endemic setting where ongoing parasitemia is inhibiting vaccine potency and life-long exposure diminishes the capacity to respond to malaria antigens. *Richie et al., Expert Review of Vaccines (2023)*
8. The next time could be much worse than this time. *Farlow et al., Vaccines (2023)*
9. The two enlargements of sympathy that are needed are: first, to feel sympathy even when the sufferer is not an object of special affection; secondly, to feel it when the suffering is merely known to be occurring, not sensibly present. It may go so far as to enable a person to be moved emotionally by statistics. *Bertrand Russel, Education and the Good Life (1926)*
10. Why we need controlled human infection models: “Mice lie and monkeys exaggerate.” *David B. Weiner PhD, The Wistar Institute, Philadelphia, USA*
11. Sed quis monebit ipsos monitores? (But who will monitor the monitors?)
Adapted from Juvenal, Satire VI (late 1st or early 2nd century)
12. De ‘90/10-gap’ treffend verwoord: “Twee derde van de wereld lijdt honger maar wij hebben ‘Pedigree Breath Busters’ — dat zijn brokjes voor honden die uit hun bek stinken!” *Theo Maassen, Functioneel Naakt (2002)*