EXTRACT FROM *CHOLERA: THE AMERICAN SCIENTIFIC EXPERIENCE 1947-1980*
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De's Successors

We have seen that in the meantime, in 1959, S. N. De of Calcutta very clearly demonstrated the existence in cholera culture filtrates of an exotoxin that mimicked the symptom of cholera that was responsible for all the ill effects of the disease, namely, the outpouring of fluid into the gut. In other words, cholera, like diphtheria and tetanus, was an exotoxinosis. But the significance of De's discovery was not immediately grasped, and his historical paper went unnoticed for some years, even, apparently, in the PSCRL.* Cholera toxin may have been discovered in 1959, but its existence was not recognized until five years later, through the work of R. A. Finkelstein at WRAIR** in Washington, and of J. P. Craig at the PSCRL. Finkelstein's paper in the *Journal of Infectious Diseases* was received by the editor in October 1963 (before Craig had started his work) and was published in June 1964; Craig's paper in *Nature* was published in August 1965; both investigators reported their findings at the second SEATO*** Cholera Research Symposium in Honolulu in January 1965, the report of which was published at an unspecified time later. Finkelstein thus has every right to claim priority (and, as we shall see, greater relevance of his work to the disease), yet it was Craig's work that was first recognized and exploited by the cholera establishment (the word is not intended in a derogatory sense) in America. This was perhaps due to three factors: Craig's work was done at the PSCRL, the institution of the establishment's making; it was simpler to assay the toxin and the antitoxin – to put it through the toxinologists' hoops – by the means that Craig had devised; Finkelstein in his younger days was highly endowed with ability, but with more than his fair share of self-assuredness, and this may have abraded his well-established elders.

In 1963, Finkelstein set about his classically important work which was to lead to the purification and crystallization of the diarrhoea-inducing cholera exotoxin, to which he gave the name "choleragen". He did this work with the *Vibrio cholerae* Inaba serotype strain 569B supplied by Dutta – the strain originally used for the Haffkine vaccine and now universally used for cholera toxin production. He started with a filtrate of ultrasonically disrupted organisms grown in a peptone medium. This is curious, since Formal maintains that "while Dutta's toxin was a sterile whole cell lysate, Finkelstein kept insisting that it was present also in culture supernatants". Indeed, he soon redirected his attention to culture supernatants. "It was considered that the active principle might be elaborated by the cell during growth and be found in good amount in the culture medium", he stated in his paper, as if De never existed. Yet he refers to De's "encouraging results – with enterotoxic filtrates of 5% peptone-water cultures", but dismisses them in the introduction since they proved to "not be entirely reproducible" (S. B. Formal, personal communication, 1979).

*PSCRL — Pakistan-SEATO Cholera Research Laboratory.
**WRAIR — Walter Reed Army Institute of Research.
***SEATO — South East Asia Treaty Organization.