The identification of Hall as a spy changes our perspective on some of the other characters in the story. David Greenglass, whose evidence formed the basis for the charge brought against the Rosenbergs, emerges from this book as an even more insignificant figure (from the point of view of espionage) than he had already seemed. This makes Julius Rosenberg a very marginal figure in the actual business of atomic espionage, and there is no good evidence that Ethel was involved.

The book leaves many questions unanswered. When did the FBI definitively identify Hall as a spy? Was he debriefed, and given immunity in return for information? Who were the still unidentified Soviet spies "Kvant" and "Pers"? There are enough such questions left to ensure that this will be by no means the last book on Soviet atomic espionage.

MICROBIOLOGY

Tales of Terrible Toxins

Michael Young

The Clostridia: Molecular Biology and Pathogenesis. JULIAN I. ROOD et al., Eds. Academic Press, San Diego, 1997. xviii, 533 pp., illus., + plates. $80. ISBN 0-12-595020-9.

The genus *Clostridium* contains many pathogenic bacteria, including the species responsible for botulism and tetanus, plus a large number of harmless saprophytes. This book, which owes its existence to The First International Meeting on the Molecular Genetics and Pathogenesis of the Clostridia (January 1995), deals almost exclusively with the pathogens.

The pathogenic clostridia do not elaborate either invasins or adhesins, proteins typically associated with a pathogenic lifestyle. Some are probably sheep in wolves' clothing, saprophytes, which produce a range of extracellular hydrolytic enzymes and become opportunistic pathogens only in environments in which they are not normally found. Even without invasins and adhesins, the pathogenic clostridia are truly remarkable for the extraordinary range—and potency—of the toxins they elaborate. This book successfully integrates basic and clinical research dealing with the production, properties, mode of action, and potential uses of clostridial toxins—as well as the diagnosis, etiology and prevention of clostridial toxemias and infections.

The exquisitely potent neurotoxins produced by *Clostridium botulinum* and *Clostridium tetani* are by far the best known clostridial toxins, and several contributions focus on botulism and tetanus. These describe therapeutic strategies for intoxicated individuals, the mode of action and medical uses of tetanus and botulinum neurotoxins, and the genetic basis and molecular biology of toxin production. One of the book's highlights is a consideration of the biochemical interactions between these toxins and their targets, from which much has been learned about the proteins that control the release of neurotransmitters from pre-synaptic vesicles.

Clostridium perfringens wreaked havoc in the trenches during World War I, because soil-contaminated wounds frequently became infected, leading in those days almost inevitably to gas gangrene. This infamy plus its rather well-studied genetics earn it a prominent place in this volume. The physical map of the C. *perfringens* genome was constructed long before that of any other Gram-positive bacterium (*1*). Several chapters are devoted to genetic analysis, genome architecture, and characterization of some of the multiplicity of toxins it produces. Preeminent among these is the hemolytic α-toxin, which is a phospholipase C. The cardinal role played by α-toxin in C. *perfringens* infections has been established in many different ways, most recently by gene replacement methods. This same methodology has undermined somewhat the widely held belief that θ-toxin (perfringolysin O), which closely resembles the thiol-activated cytolysins of other bacteria, also contributes significantly to the pathogenesis of this organism. The importance of the many other C. *perfringens* toxins (β, ε, κ, ι, λ, and μ) in pathogenesis remains to be evaluated critically. Fortunately, gas gangrene is now comparatively rare. Food poisoning, however, is quite commonly caused by enterotoxin-producing strains of C. *perfringens*, and there is currently considerable interest in the mechanism of action of that sporulation-associated protein.

Clostridium difficile, the causative agent of pseudomembranous colitis, is another intensively studied organism. This species has the distinction of producing the two largest known bacterial toxins. These proteins, toxins A and B, closely resemble each other, and the genes that encode them lie in close proximity on the bacterial chromosome. The carboxyl terminal third of both molecules contains multiple repeating units that mediate receptor binding. Another of the book's highlights is a description of the mechanism whereby toxins A and B interfere with the normal functioning of the small GTP-binding protein RhoA by specific glycosylation, which prevents RhoA from regulating cytoskeletal assembly.

The book also discusses other, less well studied, members of the taxonomically diverse clostridia. Among them, *Clostridium spiroforme* produces a binary ι toxin, which interferes with cytoskeletal assembly, and *Clostridium septicum*, which elaborates a pore-forming toxin, shows swarming behavior as part of its pathogenic lifestyle.

In spite of years of study, information about the control of clostridial toxin production is still sparse. Some progress has been made in C. *perfringens*, with the discovery of regulators similar to those that govern the synthesis of virulence factors in other pathogenic organisms. These include the putative proteins PfoR (which specifically activates its cognate for the gene encoding θ-toxin), and VirR (a response regulator) and VirS (a sensor histidine kinase), which are global regulators of toxin production. There is also evidence that a small molecular weight substance can effect intercellular signaling and lead to enhanced toxin production in these bacteria.

One common theme emerging throughout this volume is that many of the clostridial genes encoding toxins are associated with mobile genetic elements: transposons, insertion sequences, plasmids, or bacteriophages (or remnants thereof). Another is that there remains ample scope for more fundamental and applied research on this fascinating and diverse group of organisms.

The toll of tetanus. Sir Charles Bell's portrait (*c.* 1821) of a soldier wounded in the Peninsular War in Spain and suffering from generalized tetanus.

Reference

1. B. Canard and S. T. Cole, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 6676 (1989).

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