OVERVIEW OF BACTERIAL TOXINS WITH A NONREDUCTIONIST APPROACH TO THE MODE OF ACTION OF BOTULINAL NEUROTOXIN

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INTRODUCTION

The word toxin was first used in 1886 by E. Ray Lankester in *Science* to name poisons for animals produced by pathogenic bacteria. Since the word was first applied to substances which later proved to be proteins, historical precedence would demand its restriction to bacterial proteins responsible for animal pathology. An implied characteristic of these proteins is that their poisonous character can be neutralized by specific antitoxins. While toxin is used in this sense, it more commonly designates any poison for plant or animal produced by a living organism while the generic term for any harmful substance of biological or nonbiological origin is poison. Poison the older term was first used in 1579. It is meaningful to record the first use of words concerning poisonous actions as a measure of the slow progress of knowledge of toxins until the end of the 19th century: toxicology, 1799; toxication, 1821; toxicosis, 1857; toxicity, 1881; toxicant, 1882. These dates are recorded in the Oxford Universal Dictionary on Historical Principles.

The Occurrence of Toxins and Food Poisoning

A recent estimate of the number of discovered bacterial toxins is 220 by Alouf. Gram positive organisms produce 105 and gram negative organisms 115. Of these only 13 have been crystallized.

The known genera of bacteria causing food poisoning are *Salmonella*, *Shigella*, *Escherichia*, *Pseudomonas*, *Aeromonas*, *Vibrio*, *Pleiomonas*, *Listeria*, *Yersinia*, *Campylobacter*, *Bacillus* and *Clostridium*. While specific toxins have not been identified as the root cause of pathology in all of these cases, a reasonable ambition of bacteriologists is to be able to do so.

There are marked differences in the incidence of reported food poisoning caused by species of these genera, and these vary among nations. The nature of foods and their capacity to harbor and support the growth of pathogens and synthesis of their toxins, and the existence of a suitable physical environment are the determinants of the potential for food poisoning to occur. Obviously the opportunity for food to be in contact with the habitats of toxin-producing bacteria before and after marketing is a primary risk factor. Habits of community and family sanitation, personal hygiene, practices of food storage and techniques of cooking are associated risk factors.
In light of the number of toxigenic bacterial species known, what opportunities remain for the discovery of new kinds of food poisoning? Certainly with any change in food processing and packaging there is opportunity for new factors to enter into the equation of food safety.

Historically the search for a food poisoning toxin is to wait for an event of poisoning to occur, and then to seek for a causative toxin. Based on the sophistication of present scientific knowledge is it not timely to deduce from known properties of microbial growth and toxin production the likelihood of situations apt to reveal as yet unknown bacterial food poisons? Let me give an example of such a possibility. Theoretically any household use of long term refrigeration without all the water in foods turning to ice should result in sufficient growth of hitherto unrecognized cryogenic bacteria to accumulate toxins harmful on ingestion. This possibility is sustained by knowledge that candidate bacteria for this situation include *Pseudomonas* organisms. *Pseudomonas* organisms inhabit soils and surface waters making them frequent contaminants of foods, are producers of a variety of toxins, and are prominent among cryogenic bacterial species. Trial and error research on growing cryogenic bacteria in refrigerated foods in a search for new sources of food poisoning may be intellectually low key. But in human affairs the unexciting when mundane, that is, of this earth, is not always without reward.

To stay a charge of simplistic reasoning in sponsoring a trial and error approach, we recognize the deductive process in seeking for new food poisonings must be multifactorial analysis. Let me give an example. Mushrooms have been traditionally grown on soils with horse manure. The horse is a notorious shedder of intestinal *Clostridium tetani*. One might deduce from this fact that mushrooms are a source of tetanus by oral toxicity. Yet this does not appear to be so. Why? Probably because the habits of preparation for consumption of mushrooms do not permit sufficient growth of tetanus organisms with accumulation of toxin. Additionally, it appears the tetanus organisms do not compete successfully against other anaerobes for growth in the human colon and possibly in foods. Yet we should not dismiss entirely the possibility that in a rare concatenation of events the tetanus organism is found to cause a food poisoning. In conclusion we recognize the mere presence of a toxin producing organism is not of itself a sufficient condition of food poisoning.

In decay of flesh foods, numerous bacterial species, including anaerobes, participate. Do human habits of consumption which treat such spoiled foods as gustatorially and esthetically unattractive blind us from knowledge of new toxins to be acknowledged? A significant scientific problem of toxicology which remains almost ignored is the physiological and biochemical bases for the apparent immunity which permits carrion feeding animals to subsist without apparent harm on what should be toxin loaded food sources. Research on this subject might reveal as yet unknown mechanisms of resistance to toxins,