Ilya Mechnikov, Probiotics and the Health of Shellfish

*By Michael A. Rice**

In the biomedical and public health literature over the last decade there has been a rediscovery of the work of Russian microbiologist and immunologist Dr. Ilya Mechnikov (Fig. 1) who is credited with formulating the theory that beneficial microorganisms in human intestines could ward off bacterial diseases such as typhoid (a *Salmonella* disease) and cholera (a form of vibriosis), and that swallowing beneficial bacteria would make one healthier. From food preservation experiments at the Pasteur Institute in Paris, he knew that lactic acid could prevent milk from spoiling, turning it into a yogurt-like product. He wrote, "As lactic fermentation serves so well to arrest putrefaction in general, why should it not be used for the same purpose within the digestive tube?" He found Bulgarian bacilli (now known as *Lactobacillus delbrueckii* subsp. bulgaricus), that was widely used by farmers Eastern Europe to make yogurt, to be effective in inhibiting disease bacteria in the human gut. He also suggested that the culture could be taken in the form of a pill, thus anticipating the lucrative commercial probiotics craze of today. Mechnikov's big idea was that proper manipulation of the intestinal flora was the immune response of the human host, and that this was helping to battle diseases that had plagued humans for millennia. This major insight led, in part, to his co-award of the Nobel Prize in Medicine in 1908.

Figure 1. Ilya Ilyich Metchnikoff in 1908 at the time of his award of the Nobel Prize in Medicine. Photo originally from the Nobel Committee, 1908, cropped from the copyright expired version in *Wikimedia Commons*.

Unfortunately, as time moved forward Mechnikov's brilliant notion got pushed off to the side and was considered a pretty much 'fringe notion' for much of the 20th Century as the discovery and use of antibiotics arose, and scientific focus turned toward the elimination of bacterial pathogens. Striving to maintain "pathogen free" environments came into vogue. I'm sure more than just a few of us can remember our mothers admonishing us about the dangers of germs lurking just about everywhere! The medical response to any bacterial disease was to immediately turn to the antibiotics, because they worked every time, the miracles of modern medicine that they were. It was not until 1959 when the first antibiotic (tetracycline) resistant bacterium *(Shigella)* was discovered, and in the following decades, an avalanche of different antibiotic resistant bacterial strains had emerged creating great concern and anxiety within the medical and public health communities. It was not really until the mid- to late 1980s that the importance of microbiological ecology came to be truly recognized as a legitimate mainstream biomedical concern and that Mechnikov's ideas were seriously revived as

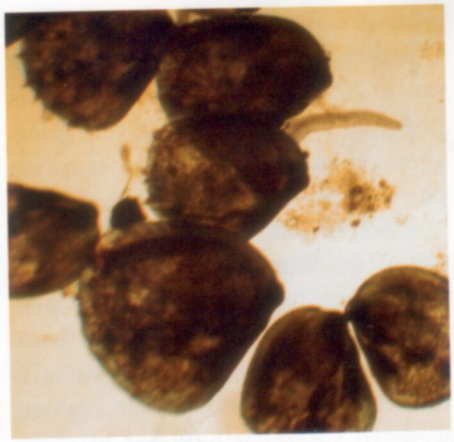

Figure 2. *Tridacna gigas spat.* Photo by Richard Masse.

a means to avert disaster as more and more antibiotics became ineffective.

In the shellfish culture world, antibiotics were also used for the treatment of bacterial diseases, particularly in hatcheries [See: Davis and Chanley (1956), *Proceedings of the National Shellfisheries Association* 56:59-74]. The use of antibiotics in hatcheries around the world was reviewed extensively by LePennec and Prieur in 1977 (See: *Aquaculture* 12:15-30) and they proposed standard protocols for antibiotic usage, because even then there was a recognition that antibiotics were often losing their efficacy as a treatment solution for many bacterial diseases. Additionally, the practice of treating seawater with ultraviolet irradiation and ozone was promoted at the time as a means for eliminating bacteria and providing "pathogen free" environments for shellfish larvae and freshly settled juveniles to grow and thrive [For example see: Blogoslawski et al., (1978). *Proceedings of the World Mariculture Society* 9:587-602]. The ideas for these treatments were in perfect harmony with the mainstream understanding about the nature of disease control at the time and it all worked as long as the antibiotics remained effective and producers were lucky enough not to have a pathogen slip through to exploit all those vacant microbiological niches opened up by the broad spectrum disinfection processes.

However, in more recent years the importance of beneficial marine bacteria filling ecological niches that might otherwise be exploited by opportunistic pathogenic bacteria is now becoming a much better understood concept. Overuse of antibiotics or overuse of indiscriminate disinfectant treatments that eliminate virtually all bacteria from molluscan hatchery systems may actually be counterproductive in the long run.

Research in the last decade has shown that various probiotic strains of marine bacteria can offer considerable protection to shellfish larvae presented with pathogenic bacterial challenges. For example in 2011, Diane Kapareiko and co-workers at the NOAA Fisheries Shellfish Laboratory in Milford Connecticut reported that they had isolated a benign strain of *Vibrio* bacteria (OY-15) from the digestive tract of oysters that can successfully protect developing bivalve larvae from bacterial pathogen challenges [See: *Journal of Shellfish Research* 30:617-625 (2011)]. Likewise Murni Karim and co-workers at the University of Rhode Island isolated a strain of *Phaeobacter* sp. (S4) from the inside of an oyster shell and a strain of *Bacillus pumilus* (RI06-95) from a marine sponge, both of which were capable of offering considerable protection to larval and juvenile oysters from the pathogens responsible for Roseovarius Oyster Disease (ROD; formerly known as Juvenile Oyster Disease or JOD) and larval vibriosis caused by *Vibrio tubiashii* [See: *Journal of Shellfish Research* 32:401-408 (2013)]. And experimental evidence suggests that the probiotics induce greater immune response by the oysters themselves.

It is likely that we are only at the dawn of the age of probiotic use in shellfish aquaculture and it is also likely that new and more effective strains of probionts will be isolated as time goes on. Efforts are underway to develop some of these known oyster probiotic strains into commercial products available for use by hatchery operators interested in adjusting the balance of microbiota in their bivalve production systems, just as Ilya Mechnikov had advocated for colon health over a century ago.

Figure 3. Bivalve hatchery. Photo by Richard Masse

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