

# A Shot in the Arm or a Hard Pill to Swallow?

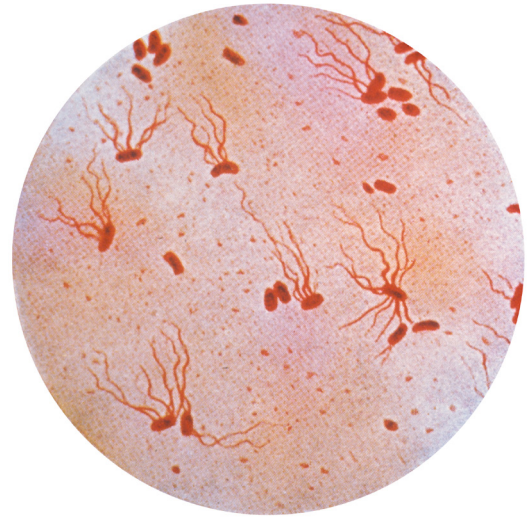
## Comparing Vaccine Formulations

by

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### Part I – The Options

The students in Dr. Stanley's course were very excited about their upcoming trip to Nepal to take samples from villagers to study *Chlamydia trachomatis* eye disease in native populations. The tickets were purchased and the accommodations booked. They had gone to the Centers for Disease Control and Prevention (CDC) website and looked at the travelers' health page for Nepal and discovered they needed two vaccines that weren't routine, one for hepatitis A and the other for typhoid fever. There was only one hepatitis A vaccine, a formalin-inactivated version of hepatitis A virus (a "killed" vaccine) given by subcutaneous injection. But there were two recommended vaccine options for typhoid fever. One of the vaccine options was a subunit vaccine, consisting of a capsular polysaccharide called Vi, from the causative agent of typhoid fever, the bacterium *Salmonella enterica* serovar Typhi (hereafter designated *S. Typhi*). This vaccine is given by intramuscular injection. The second vaccine option was a live, attenuated version of *S. Typhi*. The "modified live" vaccine is a strain of *S. Typhi* that has multiple mutations, including ones in genes encoding the biosynthetic pathway for production of the Vi capsule. This vaccine is given as enteric-coated capsules. The students with a fear of needles thought that an oral vaccine sounded better, but the idea of eating live bacteria on purpose, even as part of a vaccine, didn't sound so great either.

Dr. Stanley told the students they should get out their textbooks to help them understand the kind of immunity each vaccine would give them so they could decide which vaccine would be best for a pathogen like *S. Typhi*, which has the following properties:

- The organism is spread by the fecal-oral route (i.e., it is acquired by ingesting food or water contaminated with the bacteria) so it enters via a mucosal site.
- The organism enters host cells and lives within these cells so that it is "hidden" from extracellular defenses.
- The organism enters the bloodstream where it multiplies and spreads to other tissues.

Before they looked up the different kinds of vaccines, he suggested they answer the following questions.

### Questions

1. What is an antigen?
  
  
  
  
  
  
  
  
  
  
2. What are the two different types of adaptive immunity?

3. Why does it take one to two weeks for adaptive immunity to be induced the first time the body sees an antigen?
4. Why does it take a much shorter time for adaptive immunity to be induced on subsequent encounters with the antigen?
5. What cells are antigen-presenting cells?
6. What is meant by “antigen presentation,” and how do antigen-presenting cells present antigens?
7. How do T cells recognize antigen?
8. What type of antigens do T cells recognize (i.e., what types of molecules and what is their molecular nature)?
9. What do helper T cells help?
10. How do cytotoxic T lymphocytes recognize cells to kill?
11. How do cytotoxic T lymphocytes kill cells?
12. What is the relationship between antibodies and B cells?
13. How do B cells recognize antigens?
14. What types of antigens do B cells recognize (i.e., what types of molecules and what is their molecular nature)?
15. What are the functions of IgG antibodies?
16. What is the main function of secretory IgA (sIgA)?
17. What feature of antibodies results in their ability to cross-link antigens?

## Part II – The Choice

Dr. Stanley said that now that the students had answered questions to make sure they knew a little about the immune system, it was time to figure out which vaccine to use. First, they needed to go to the vaccine chapter so they could be sure they knew what different types of vaccines are currently available. Using the online resource from the NIH and the following information they could learn a little bit more about the various types of vaccines:

- Inactivated (“killed”) vaccine
  - Intact, non-living organisms
    - Physical inactivation: heat, uv,  $\gamma$ -irradiation
    - Chemical inactivation: formalin, phenol, iodoacetate
- Subunit vaccine
  - Highly concentrated purified versions of molecules from microorganisms, including toxoids (detoxified toxins)
  - Typically given with an adjuvant
  - Conjugate vaccines: linking of a polysaccharide to a protein to stimulate T-cell processing of the antigen
- Modified live vaccine (live, attenuated)
  - Live organisms modified so they cannot cause disease
    - Attenuated during *in vitro* serial passage by base-pair mutations or deletions
    - Genetic engineering to provide more rational methods to develop live attenuated vaccines

Dr. Stanley reminded the students that people get infected with *S. Typhi* either by eating food or by drinking water contaminated with the bacteria. These bacteria then cross through the intestinal epithelium and are taken up by macrophages in which they multiply. The bacteria then spread via the bloodstream to other tissues.

### Questions

1. What is an adjuvant?
2. Draw a diagram to show the main steps in the development of the immune response that occur after exposure to a subunit vaccine delivered by intramuscular injection. Using this diagram, predict what kind(s) of immune response (antibody-mediated [humoral], cytotoxic T cells [cell-mediated] or both, systemic and/or mucosal) this vaccine would likely give.
3. Draw a diagram to show the main steps in the development of the immune response that occur after exposure to a modified live vaccine given orally as enteric-coated capsules. Using this diagram, predict what kind(s) of immune response this vaccine would likely give.
4. Draw a diagram to show the main steps in the development of the immune response that occur after exposure to a killed vaccine given by subcutaneous injection. Using this diagram, predict what kind(s) of immune response this vaccine would likely give.
5. What are some disadvantages of a subunit vaccine?
6. What are some disadvantages of a modified live vaccine?
7. What are some disadvantages of a killed vaccine?
8. Which typhoid fever vaccine would you recommend the students get before going off to Nepal? Justify your choice.