HST.939 Designing and Sustaining Technology Innovation for Global Health Practice
Spring 2008

Lecture 3: 2/19/08

Discussion of projects; administrative information on how to start off.
Split into assigned groups to discuss the projects.

Dr. Langer's lecture

Controlled drug delivery

- how he got into it
- some of what he's done
- how it fits into global health

Background: chem. E as undergrad; graduated 1974. Energy crisis then; had to wait in line for gas. This lead to many job opportunities as a chemical engineer. But he wasn't that interested in making more efficient gas – he was interested in education, but wasn't hired by any schools. Interested in medicine – but no hospitals hired him either, until a Dr. Folkman who was interested in anti-angiogenesis as a way to create dormant tumors took Langer on to help with his research. So, he was involved for awhile in angiogenesis and cancer research.

Biotechnology was a developing field; it was very difficult to figure out how to deliver macromolecules like polypeptides to a human system chronically and at steady rates, due to their size and short half-lives. Figured out how to deliver these molecules through polymers (slow-release). Used this to test induced/repressed angiogenesis in a rabbit cornea; could induce angiogenesis with or without an inhibiter, and saw dramatic differences.

Delivering polypeptides with polymers is commonly used today as treatment for many different problems that require supplementation of a protein.

Drug delivery chip – size of a dime – in which are wells that hold drugs inside them, not to be released until receiving an electrical signal.

Discovery of materials to be used for medical purposes often came from observing everyday objects and materials with similar material properties, for example:

- artificial heart material: polyether urethane, originally in ladies' girdles
- dialysis tubing material: cellulose acetate, originally from sausage casing
- etc.

Biodegradable polymers: there are optimal, and potentially terrible, modes of erosion.

- bulk erosion: holes progressively form, non-uniform pattern throughout material, leading eventually to entire material breaking down all over and releasing all of its drug at once. Could have terrible consequences, depending on drug.

- Surface erosion: outer layers erode first, uniformly, until nothing is left. Predictable, steady degradation/drug release.

Reviewers criticized the method and refused funding because:
- polymers cannot be synthesized (‘81)
- polymers will react with their drug (‘83)
- polymers are fragile (‘85)
- polymer-drug system would be toxic (‘86)
- drug will not diffuse far enough to kill whole tumor (‘88)
- poor drug, anyway (‘90)
- drug delivery systems cannot be manufactured (‘93)

FDA finally approved this method in 1996.

Plastics with memory – different shapes determined by different temperatures.
(Examples: plastic string forms loose knot in air, knot tightens when dropped into body-temperature water; plastic string is loose in air, tightens into a uniform coil when dropped into body-T water).

Aerosols:
Difficulties with pulmonary delivery systems; particles aggregated together. Developed an optimal size for deep lung deposition – has the same mass as previous particles, but is larger in size and less likely to aggregate with others (added holes, basically).

Organ transplant alternative:
Create biodegradable polymer scaffolding upon which human cells can grow; form new organs, for example, or can be used in plastic surgery (grow a particularly-shaped new nose).
- Can create synthetic small blood vessels with many of the properties of real blood vessels, but where do you get the original vessel cells from? Human endothelial cells can form functional blood-carrying vessels.
- Synthetic skin
- Scaffold of spinal cord; some success in regrowing cord in rats and restoring function to paraplegic rats
- Ongoing experiments to regenerate weight-bearing, articulate cartilage