Biology 446 October 5, 2016

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**I)** **Discuss the possibility** (and evidence pro and/or con) **that atherosclerosis could be caused by an autoimmune attack on some protein** that only occurs in arteries. What if treatment with cortico-steroids and other inhibitors of the immune system caused reductions in atherosclerosis?

**II)** Suppose that atherosclerosis is partly caused by mutations in one or more of a few genes.  **Please hypothesize the normal functions of genes that can cause atherosclerosis when mutated**. (Enzymes?, That catalyze what? Signal molecules? Adhesion molecules? Something else? Maybe a component of the immune system?)

**III)** **Would you expect an additive relation in the genetic causation of atherosclerosis?** (In the sense that having two of the mutations would double the severity, having three of the mutant genes would triple the severity; etc.) What could you learn from such additive effects? What hypotheses would be confirmed?

**IV)** What **if having a combination of two such mutations** (both of which worsened atherosclerosis) **resulted in no worse symptoms than either mutation alone**.

**Could you deduce anything** about how the genes or their normal functions are related to each other?

**V)** **What if such a combination of mutations produced ten times worse symptoms**, as compared with either mutation alone. Can you invent a hypothesis that would predict that?

**VI)** Please consider whether **genetic difference that favor development of atherosclerosis** (Cause worse symptoms? Earlier onset? More fatality?) **would be expected to be dominant? Recessive? Co-dominant?** Is the answer to this question related to the additivity of effects of different mutations?

**VII)** **If atherosclerosis is made worse by mutations in a certain gene**, will **deletion of that gene cause even worse effects?** (Or could this be true for some genes, while deletion of other genes could have the opposite effect, i.e LESS severe atherosclerosis?) Could answers to such questions be useful, medically?

**VIII)** Imagine that genes which affect atherosclerosis turn out to differ in these respects, **some being dominant, others being recessive. Can you deduce anything** about how such genes serve their normal functions?

**IX)** When you increase the pressure inside a pipe or an artery, does this increase the mechanical tensions in their walls? (Hint: sure it does.) Will these increased tensions be stronger in the direction along the length of the tube?

Or will stronger be created in the circumferential direction? Does the answer to this question differ depending on what material the pipe is made of? Does it matter whether the walls or arteries are actively contractile?

**X) When a vertebrate animal grows in overall size**, this requires and includes increasing the diameters and lengths of its arteries. **Which of the following changes cause these increases in artery size?** Elongation of individual smooth muscle cells? Secretion of more collagen fibers? Reduction of contractile strengths of circumferential cells (of smooth muscle cells, of non-muscle cells, of both?)

**XI)** **When an artery doubles in circumference?** The tension in its smooth muscles also doubles? The tension decreases? The tension stays the same? The answer depends on the contractility of its circumferential smooth muscle cells? The answer depends on properties of collagen fibers in the artery wall? Something else?

**XII)** **Suppose you invented a relatively non-invasive method to induce elongation of the outer layers of atherosclerotic arteries**, and that didn't cause elongation in areas where thee was little or no "plaque": Could you use this method to treat atherosclerosis? Describe what you would try doing?

**XIII) For the purpose of curing coronary blockage**, what changes in which properties of what cells would you estimate should be most useful?

**XIV) Why doesn't increased blood pressure just push atherosclerotic plaque out of the way, thereby opening a wider path?**

**XV) Can we learn anything about the relative strengths, tensions and pressures** of different parts of atherosclerotic plaques, by looking carefully at cross sections?

**XVI) What would be the most interesting** (&/or medically useful) fact to learn about atherosclerosis?

**XVII) True of false: "You are as old as your arteries"!**

**XVIII)** Joggers and others **who expect exercise to improve the strengths and stamina of their heart, arteries, bones and other tissues must be assuming some general principle** about the normal mechanisms that regulate tissue growth. Or are they just trying to loose weight? What general principle do they assume? Is it true?

**XIX) Hint**: How many people try to improve the strengths of their cars by driving faster up mountains?

**XX)** Yes/No/Sometimes/Maybe: Embryological mechanisms that build anatomical structures can also serve to repair them, and to prevent their degeneration? Or is the opposite true?