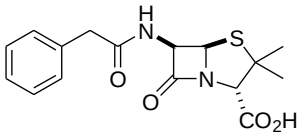
BPS 2110 Intro to Biopharm
Mid Term 2 Answers

1) Complete the following table describing pathogen classification. (**8 Points**)
(2) each line

	Risk characteristics	Type of lab protection (provide one or two)	Example of one pathogen
Class 1	- No risk or low risk (limited risk)	Open bench	E. coli
Class 2	- Moderate risk	- Limited lab access - Lab coat - Laminar hood	Herpes virus
Class 3	- High risk (death or serious illness)	- Restricted access - Gowns, gloves - Respirators - Low pressure room - Airlocks - Liquids/gases filtered - All materials exiting autoclaved and incinerated	H.I.V. Y. Pestis (plague)
Class 4	- Extreme risk (Lethal highly infectious untreatable)	- Restricted access - Low pressure room - Airlocks - Special training - "space suits" - Shower before entering/exiting - Liquids/gases filtered - All materials exiting autoclaved and incinerated	Ebola Marburg Lassa fever Hanta virus smallpox

2) This structure is the basis of most modern antibiotics.



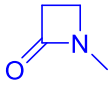
a) What enzyme does it inhibit? (**1 Point**)

transpeptidase

b) How does inhibition of this enzyme cause bacterial death? (**4 Points**)

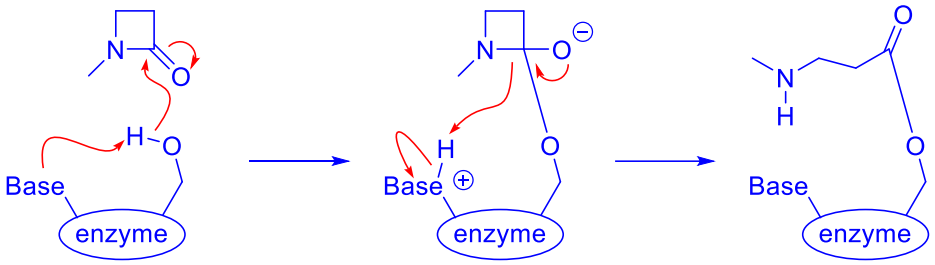
- Bacteria cannot make cross-links in cell walls
- Cell wall material is weakened
- internal pressure (osmotic) causes the cells to rupture during cell division

c) What functional group structure in this molecule is responsible for enzyme inhibition? (**1 Point**)



or β-lactam

d) Use a <u>mechanism</u> to show how this feature reacts with the enzyme to produce inhibition (**4 Points**)



e) This class of drug is very "clean" (very few side effects). Why does this drug show such a good side effect profile? (**4 Points**)

- Human cells do not have cell walls
- Transpeptidase does not exist in humans – drug has no human "target"

- Normal substrate for transpeptidase is very different from other protein structures (D-amino acids instead of L-amino acids)
- Nothing like this substrate in humans- our enzymes are very different from transpeptidase

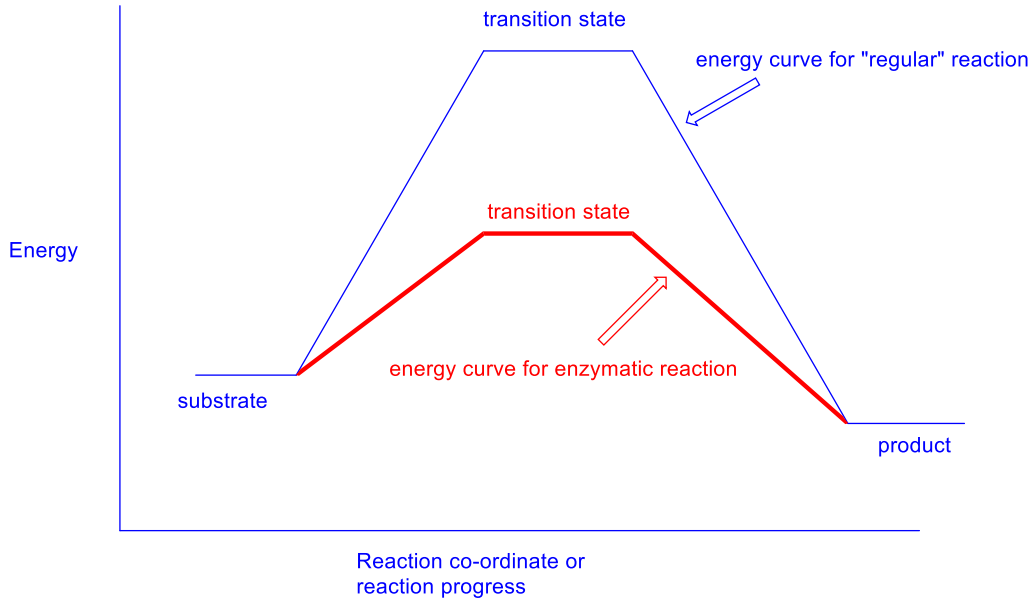
f) The major side effect associated with this class of drugs is allergy. Briefly explain how allergies to this drug arise (**4 Points**)

- Humans do have serine proteases
- May also have other proteins with nucleophilic side chains
- Penicillin is a good electrophile, may react with one of these proteins
- Creates a "new" protein which is now recognized as foreign by the body's immune system giving an allergic reaction

3) Enzymes are catalysts that carry out reactions in living things.

a) Use a reaction co-ordinate diagram to explain how enzymes are able to catalyze reactions (**6 Points**)

- Enzymes bind tightly to transition states and lower the energy of the transition state
- This lowers the activation energy for the reaction



b) What **general strategy** can be used to develop inhibitors of any enzyme? (**1 Point**)
Transition state mimic or analog

(also accept rational drug design)

c) Why does this strategy work so well? (**4 Points**)

- Enzymes bind very tightly to transition states
- Enzymes therefore bind very tightly to molecules that resemble transition states
- Can use the structure of the transition state to guide SAR

4)

a) What two enzymes does the HIV virus use to convert RNA into DNA? (**2 Points**)

- Reverse transcriptase
- RNAse H

b) What characteristics of the enzymes in part (a) contribute to the unusually high mutation rate for HIV? (**4 Points**)

- reverse transcriptase is a very sloppy enzyme
- makes lots of errors
- RNAse H destroys RNA template to make a DNA copy
- no possibility for error checking
- results in a large veriety of virus genomes (error every 9000 bases)
- virtually every virus particle is different

c) What drug strategy is used to counteract this high mutation rate (name and acronym)? (**2 Points**)

- HAART
- Highly Active Antiretroviral Therapy

5) In 2009 the H1N1 virus caused serious concern.

a) What does the designation H1N1 mean? (**2 points**)

H = Hemagglutinin

N = Neuraminidase

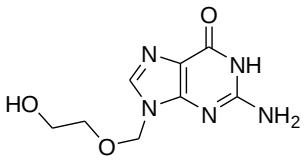
b) Why is this system used to classify influenza viruses? (**2 Points**)

- Both proteins are found on the outside of the virus envelope
- Easy to detect using antibody tests

c) Describe the general function of each of the components you identified in part a. (**4 Points**)

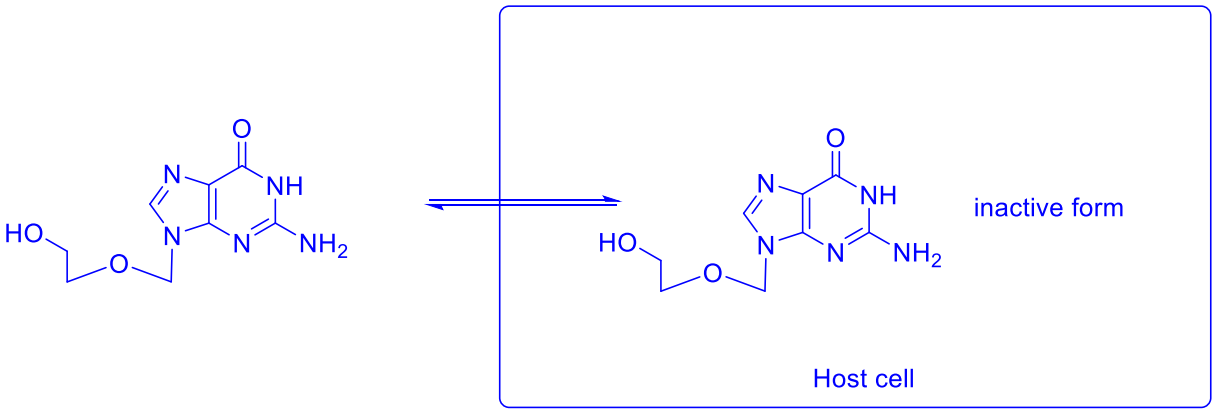
- Hemagglutinin sticks to human proteins that carry sialic acid on surface of human cells
- Binding between hemagglutinin and sialic acid allows the virus to enter cells
- Neuraminidase removes the sialic acid from human proteins on the outside of the virus envelope
- This prevents the virus particles from sticking to each other and becoming non-infectious

6) The antiviral drug Acyclovir shows an unusual pattern of bioavailability that produces a very low incidence of side effects. Describe in detail how the drug is distributed in the body and in virally infected cells. It may be helpful to use a diagram for part of your answer. (**7 Points**)



Acyclovir

Drug is not phosphorylated by host enzymes. is able to freely diffuse in and out of host cells. becuase it is not phospharylated, the drug in in the inactive form, and cannot interact with polymerases.



Drug is phosphorylated by viral enzyme. once phosphorylated, host enzymes convert the mono-phosphate into a triphosphate. this carries multiple negative charges which prevent the triphosphate from passing through non-polar membranes and out of the cell. the drug accumulates in cells (LeChatelier's principle) as the triphosphate. this is also now the "active" form that can inhibit viral polymerase.