Biochemistry on the MCAT

Watch the recording and download the presentation handout below:

http://nextsteptestprep.com/2015/07/13/biochemistry-sample-class-july-2015/

Introductions

- Dr. Anthony LaFond, MD-PhD.
- Director of MCAT Content for Next Step
- Worked with thousands of MCAT students over the last 10+ years
- Personally achieved a 42 MCAT

Agenda

- What effective MCAT prep looks like
- Practice Problems
- Passage Strategy
- Passage Practice
- Wrap up and Q&A

Fail to plan. Plan to fail.

- Content review – build a solid base.
- Practice multiple strategies – what works best for you?
- Build a countdown to test day schedule.
- Highlighting and note taking: Important throughout the exam.

Biochem Question 1

1) Enzyme B is introduced to a reaction for which the reactants are substrates to enzyme B. Which of the following will occur?

A. The forward and reverse reactions will proceed slower.

B. K_{eq} for the reaction will increase.

C. The rate at which the equilibrium is reached is decreased.

D. The rate at which the equilibrium is reached is increased.

Biochem Question 2

2) Which of the following will NOT be oxidized in the presence of $KMnO_4$?

A. t-butyl alcohol

B. Heptanol

C. 2-propanol alcohol

D. *cis*-2-pentene

Biochem Question 3

3) The carbonyl carbon is very:

A. electrophilic.

B. nucleophilic.

C. acidic.

D. basic.

Biochem Question 4

4) Rank the following molecules in order of increasing acidity.

I. $CH_3CH_3CH_2ClCOOH$

II. $CH_2ClCH_3CH_3COOH$

III. $CH_3CH_3CH_2FCOOH$

A. III< II < I

B. II < III < I

C. I < II < III

D. II < I < III

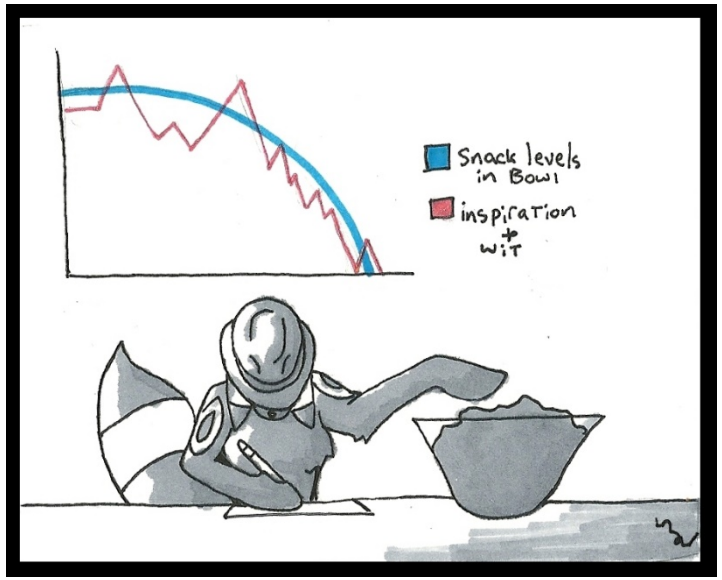
How to highlight

- Read briskly, use highlighter to capture key points!

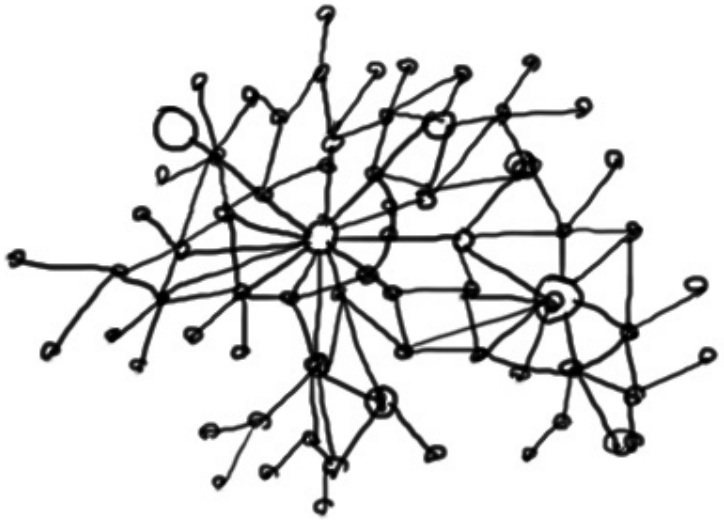
- What to look for:
  - Opinion
  - Points of contrast
  - Cause and effect!

When taking notes, focus on:

Correlations



Connections



Cause and Effect

Biochem Passage 1

Owing to its large size, the Golgi apparatus (GC) was one of the first organelles to be discovered and observed in detail. Cells synthesize a large number of different macromolecules. The Golgi apparatus is integral in modifying, sorting, and packaging these macromolecules for cell secretion or use within the cell. It is essential to the compartmentalized eukaryotic cell. Pharmaceuticals that interrupt the efficiency of the Golgi apparatus reduce cell viability and can serve as valuable cancer treatments.

ADP-ribosylation factor 3 (Arf3) is responsible for the recruitment of cytosolic coat protein complexes (COPs) and subsequent retrograde transport from the Golgi apparatus. Arf3 is activated by guanine nucleotide exchange factors, which substitutes guanosine triphosphate (GTP) for guanosine diphosphate (GDP). Upon GTP substitution, Arf3 is rearranged and releases the N-terminus of the polypeptide chain from a site in the protein and instigates their sequestration to phospholipid bilayers. Through its coupling with a bilayer, Arf3 further facilitates vesicle formation by the recruitment of the coatomer protein complex COP-1 (subunits are represented by βγδζ). The Arf3 GTPase activating protein catalyzes the conversion of Arf3-bound GTP to GDP, inactivating the protein. GTPase activity is increased by Arf3 binding to COP-1. Assays were performed to determine GTPase activity as a function of GTPase activating protein (GAP) present. In addition phosphorimages of protein-bound [α-32P] and [α-32P] GTP from incubations with the indicated amounts of ARF GAP in this experiment were performed with the results shown in figure 1.

Biochem Passage 1

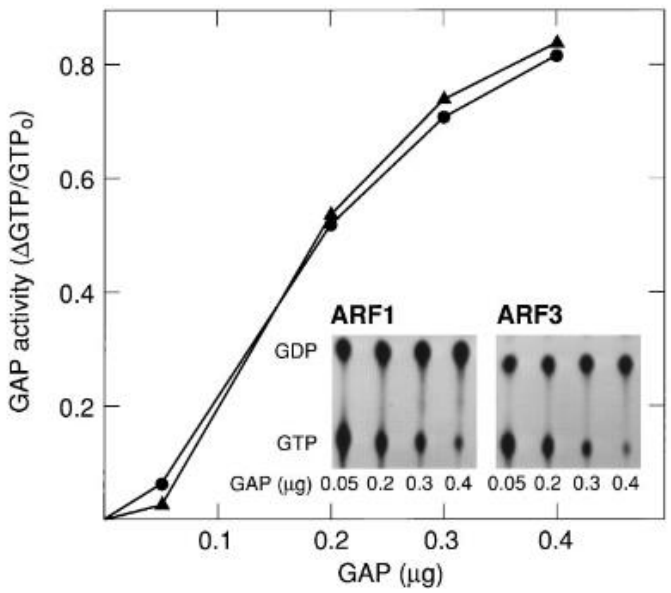


Figure 1 GAP-stimulated GTPase activity of native ARF1 and ARF3.

GTPase activity of ARF1 (•) and ARF3 (▲) each 0.15 mM, with the indicated amount of purified GAP, was determined using assay.

Angiogenesis, the formation of new blood vessels, is an essential step for cancer progression. This formation is inhibited in part by the mechanism of monensin A, an inhibitor of protein transport from the endoplasmic reticulum to the Golgi apparatus. Monensin A has been shown to reduce Arf3-driven cell surface vascular endothelial growth factor receptor (VEGFR) expression on endothelial cells in culture, resulting in reversible interruption of the Golgi apparatus and partial remission *in vitro*. Due in part to low tissue uptake, monensin A is not an effective anti-cancer agent; but, it has led to the recognition of deoxymannojirimycin (DMNJ) as a promising cancer therapeutic.

DMNJ is hypothesized to attach to a protein—protein contact interface of Arf3, preventing GTP exchange by GEF and disrupting Arf3 membrane localization in the initial critical step of COP1 recruitment and vesicle formation. In clinical settings, treatment with DMNJ has led to remission in rat models of skin cancer.

Biochem Passage 1 Questions

6) The gene products that are packaged in Arf3 -COP vesicles are most likely destined for:

A) the smooth endoplasmic reticulum.

B) the rough endoplasmic reticulum.

C) the lysosomes.

D) the nucleolus.

Biochem Passage 1 Questions

7) Which of the following is the likely outcome of hydrolysis of a ζ phosphate group from an Arf3-bound GTP?

A) Loss of primary protein structure

B) Protein-membrane binding

C) Protein activation

D) Protein inactivation

Biochem Passage 1 Questions

8) Which of the following enzymes performs a similar function to the Arf3 GTPase activating protein?

A) Pyruvate Kinase

B) Lactate dehydogrenase

C) Alkaline phosphatase

D) Peptidyl transferase

Biochem Passage 1 Questions

9) The mechanism of Monensin A described in the passage indicates that the drug would be best used to treat:

A) bacterial infection by *Bacillus anthracis*.

B) viral infection by *Varicella zoster*.

C) bacterial infection by *Salmonella enterica*.

D) fungal infection by *Candida albicans*.

Biochem Passage 1 Questions

10) GTP is classified as a member of which class of biological molecules?

A) Amino acids

B) Peptides

C) Nucleotides

D) Nucleic Acids

Integration for the MCAT

Protein Structure

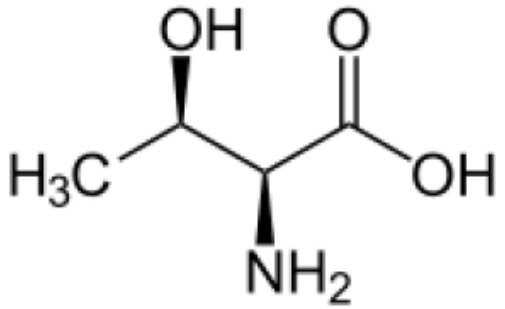
Level	Description	Stabilized by	Example
Primary			
Seconday			
Tertiary			
Quaternary			

Practice!

11) One of the problems in certain forms of Schizophrenia is a loss-of-function mutation to peptidyl transferase. What process is most likely to be halted in these patients?

A. Binding of the mRNA template to the ribosome
B. Construction of the cellular ribosome
C. Construction of the primary structure of neuroproteins
D. tRNA recognition of mRNA codons.

12) A polar-substrate binding enzyme is most likely to have threonine residues richly populating which region? :



A. The interior of the enzyme.
B. The exterior of the enzyme.
C. The active site of the enzyme.
D. Within an alpha-helical structure.

Biochem Passage 2

Voltage-gated sodium (Na_V) channels are responsible for propagating action potentials. Humans contain a complex repertoire of nine Na_V channel subtypes denoted $Na_V1.1$–$Na_V1.9$. $Na_V1.7$ plays a crucial role in the human pain signaling pathway and it is an important therapeutic target for treatment of chronic pain.

A scientist sought to determine the diversity of $Na_V1.7$-active peptides in the venom of an Australian tarantula and to characterize their potency and subtype selectivity. Three tarantula peptides were reduced and alkylated using the volatile reagent triethyl-phosphine, prior to tryptic digestion. The mass of each peptide was found to increase by 270 Da following reduction/alkylation.

Next the three peptides were isolated. TRTX-Phlo1a, -Phlo1b and -Phlo2a, inhibit human $Na_V1.7$ ($hNa_V1.7$). Phlo1a and Phlo1b are 35-residue peptides that differ by their C-terminal amino acid. The partial sequence of Phlo2a revealed extensive positively charged residues *in vitro*. Human oocytes were treated with each peptide and IC_{50} (how much of a particular substance is needed to inhibit a given biological process by half) and $V_{0.5}$ (the voltage at which the channels are half-maximally activated) was measured for each of the peptides. Phlo1a and Phlo1b inhibit $hNa_V1.7$ with IC_{50} values (mean ± S.E.M) of 439±46 and 400±61 nM, respectively, with only minor activity on $hNa_V1.5$. Although similarly potent at $hNa_V1.7$ (IC_{50} 333±19 nM), Phlo2a also potently inhibited $hNa_V1.2$ and $hNa_V1.5$.

Biochem Passage 2

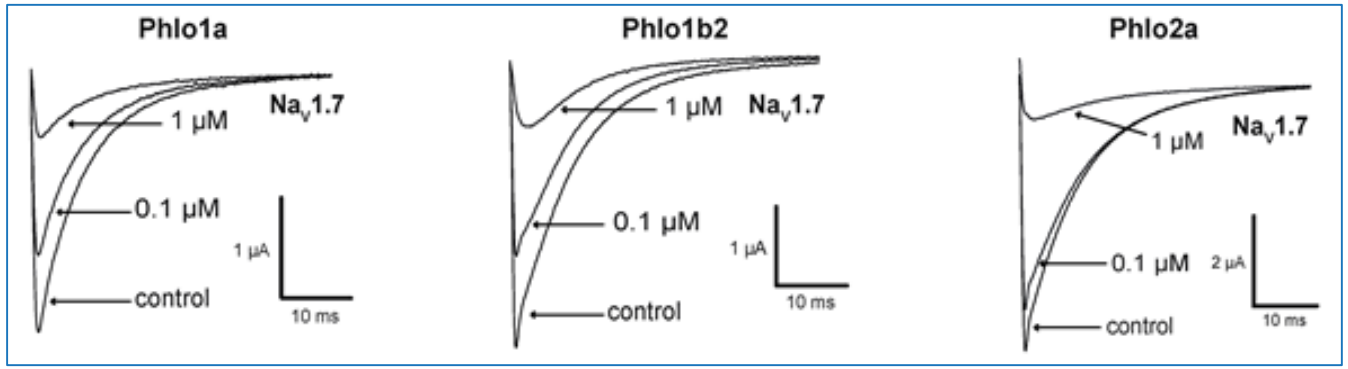


Figure 1 Effects of venom peptides on $hNa_V1.7$ expressed in oocytes

Whole-cell Na current traces were made on all three peptides in the absence and presence of 0.1 or 1 μM peptide (figure 1). Sodium currents were evoked by a 50-ms step depolarization to 0 mV from a holding potential of −80 mV every 10 s. Mean $V_{0.5}$ for the $Na_V1.7$ channel was observed to shift from -18 mV to – 12 mV and -8 mV. Concentration-effect curves for inhibition of $hNa_V1.7$ by Phlo1a, Phlo1b and Phlo2a (n = 15) were recorded as well (figure 2).

Biochem Passage 2

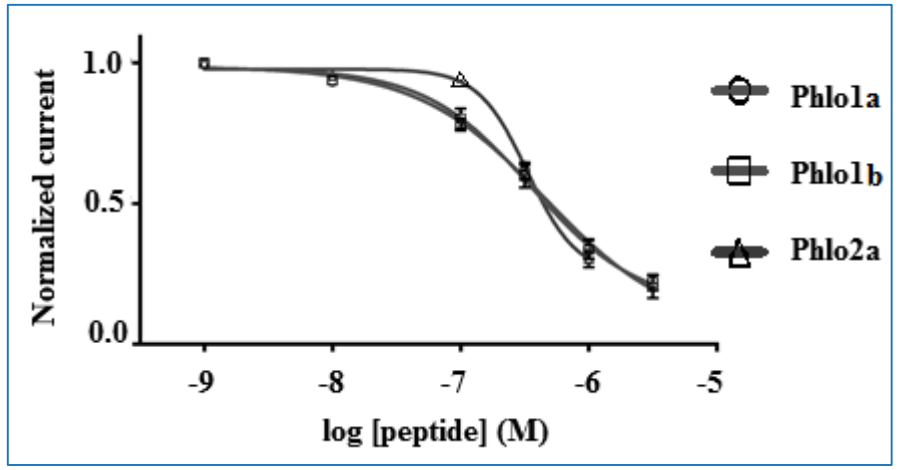


Figure 2 Concentration-effect curves for inhibition of $hNa_V1.7$

The majority of tarantula-venom peptides are 3.0–4.5 kDa in size and highly disulfide-bridged. These bridges allow them to form a highly stable knot fold that provides resistance to chemical and thermal degradation as well as proteases. Numerous spider venom peptides have been shown to modulate the activity of Na_V channels and these peptides represent a rich source of research tools and therapeutic lead molecules.

Biochem Passage 2 Questions

13) What is the effect of the spider-venom peptides on channel activity?

A. All three peptides inactivate the S4 helix in $hNa_V1.7$ channels.

B. All three peptides cause a depolarizing shift in the voltage-dependence of $hNa_V1.7$ activation.

C. All three peptides cause a hyperpolarizing shift in the voltage-dependence of $hNa_V1.7$ activation.

D. All three peptides cause the cell membrane to transition from resting to polarized.

Biochem Passage 2 Questions

14) A central aspect of developing new anesthetics is the specificity of the agent's signaling. Based on the data from the experiment, which of the peptides would be LEAST effective as an anesthetic?

A. Phlo1a

B. Phlo2b

C. Phlo2a

D. Phlo1b

Biochem Passage 2 Questions

15) Which of the following would best explain the reason for the variance observed in channel effect by the peptides studied?

A. Phlo1a has a significantly lower molecular weight than the Phlo2a and Phlo1b peptides.

B. Phlo2a has a lower IC_{50} compared to Phlo1a and Phlo1b.

C. C-terminal residues influence Na_V subtype selectivity of venom peptides.

D. Phlo2a binds to the channel at multiple sites with positive cooperativity.

Biochem Passage 2 Questions

16) Which amino acid is most likely to be found protecting the receptor binding areas on the venom peptides discussed in the passage?

A. M

B. H

C. C

D. W

Biochem Passage 2 Questions

17) Nodes of Ranvier act as relays for myelinated neuron signaling. How might the action potentials of such a neuron be affected if the intermodal distances were increased significantly?

A. Action potentials might fail to traverse the axon.

B. Action potentials might travel slower than their normal velocity.

C. Action potentials would travel faster than their normal velocity.

D. Action potentials would remain unaffected due to the all-or-nothing response.

Active Memorization

Amino Acid	3 letter Abbrev.	1 letter Abbrev.	Side Chain Property	Side Chain Structure

Biochem Passage 3

The variety of human antibodies, over 10^{12} different molecules, poses a unique genetic problem: how can a human, whose genome contains fewer than 50,000 genes, make more antibodies than there are genes in its genome? The mammalian immune system has evolved unique genetic mechanisms that enable it to generate an enormous number of different antibodies by joining separate gene segments together before they are transcribed.

Antibodies are produced from three pools of gene segments and exons. In each pool, separate gene segments that code for different parts of the variable region of the light or heavy chains are brought together by site-specific recombination during B cell development. The combinatorial joining of these segments, called *combinatorial diversification*, greatly increases this variety. Light-chain pools contain one or more constant- (C-) region exons and sets of variable (V) and joining (J) gene segments. The heavy-chain pool contains sets of C-region exons and sets of V, diversity (D), and J gene segments. A V_L gene segment recombines with a J_L gene segment to produce a DNA sequence coding for the V region of a light chain, and a V_H gene segment recombines with a D and a J_H gene segment to produce a DNA sequence coding for the V region of a heavy chain. Each of the assembled V-region coding sequences is then co-transcribed with the appropriate C-region sequence to produce an RNA molecule that codes for the complete polypeptide chain. The light chain portion of this synthesis is shown in figure 1.

Biochem Passage 3

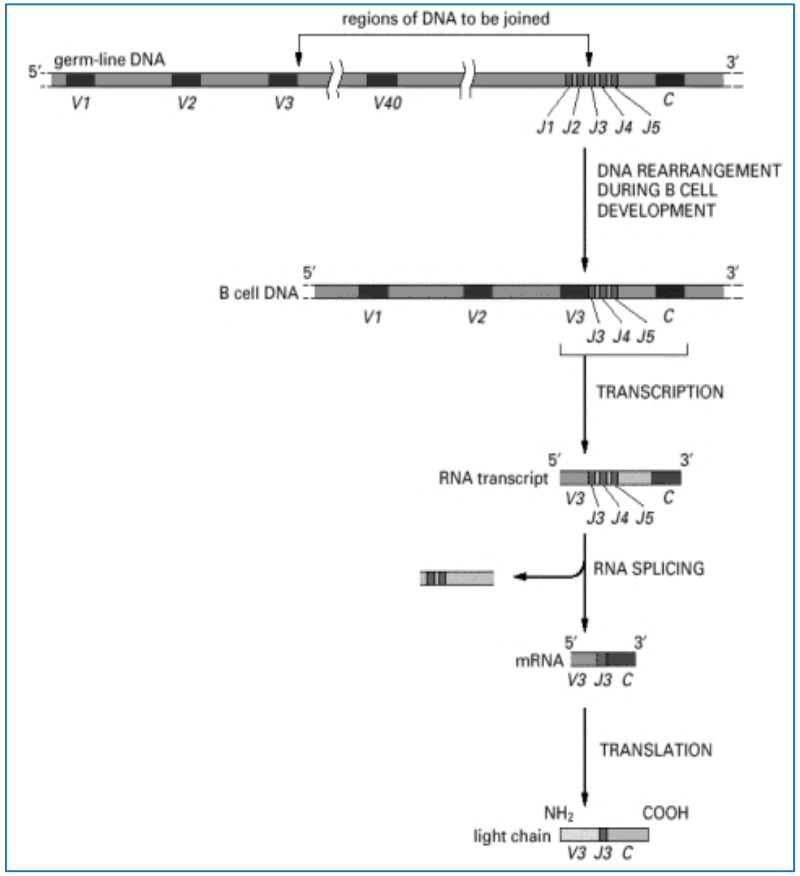


Figure 1 The V-J-C joining process involved in making a human light chain

In the "germ-line" DNA the cluster of five *J* gene segments is separated from the *C*-region exon by a short intron and from the 40 *V* gene segments by thousands of nucleotide pairs. During the development of a B cell, the randomly chosen *V* gene segment is moved to lie precisely next to one of the *J* gene segments. The extra *J* gene segments and the intron sequence are transcribed (along with the joined *V3* and *J3* gene segments and the C-region exon) and then removed by RNA splicing to generate mRNA in which the chosen *V*, *J*, and *C* sequences are contiguous. These mRNAs are then translated into light chains. A *J* gene segment encodes the C-terminal 15 amino acids of the V region, and the *V-J* segment junction coincides with the third hypervariable region of the light chain, which is the most variable part of the V region.

Because the antigen-binding site is formed where the hypervariable loops of the V_L and V_H come together, the heavy and light chains can pair to form millions of different antigen-binding sites. This number is greatly increased by the loss and gain of nucleotides at the site of gene-segment joining, as well as by somatic mutations that occur with very high frequency in the assembled V-region coding sequences after stimulation by antigen and helper T cells. After repeated stimulation by antigen, B cells will favor more effective antibodies—a process called *affinity maturation.* This process greatly increases antibody effectiveness.

Biochem Passage 3 Questions

20) The function of spliceosomes during antibody production is to:

A. cleave introns from the RNA and ligate the fragments.

B. condense the exons into smaller units.

C. induce conformational changes in the DNA to allow splicing.

D. prevent the transcription of the unused V and J regions.

Biochem Passage 3 Questions

21) According to combinatorial diversification, how many different light-chain V regions can the DNA in figure 1 produce?

A. 5 x 40

B. 40 x 5 x 15

C. 50 x 4

D. 40 x 40 x 15

Biochem Passage 3 Questions

22) Linked genes are:

A. Located on different chromosomes of the same size and shape.

B. located on the same chromosome.

C. rarely segregated to the same gamete during meiosis

D. silenced through translational repression more often than unlinked genes.

Biochem Passage 3 Questions

23) What is the most likely mechanism through which affinity maturation is able to improve the host's defenses?

A. B cells expressing lower-affinity receptors are stimulated by the antigen to survive and proliferate, whereas other B cells survive and proliferate.

B. B cells expressing higher-affinity receptors are stimulated by the antigen to survive and proliferate, whereas other B cells undergo apoptosis.

C. B cells expressing lower-affinity receptors are stimulated by the antigen to undergo apoptosis, whereas other B cells undergo apoptosis.

D. B cells expressing higher-affinity receptors are stimulated by the antigen to undergo apoptosis, whereas other B cells survive and proliferate.

Biochem Passage 3 Questions

24) Which of the following mechanism(s) for promoting genetic diversity does the human body possess?

I. Crossing over

II. Sexual reproduction

III. Spontaneous mutations

A. I only

B. I and II only

C. II and III only

D. I, II and III

Five things to remember!

Critical Analysis!

Start early to find

YOUR strategy

2

Passage analysis:

Note-taking and

highlighting

Science content: Rule of 2's

3

4

Know what to expect on test day

Study Group 5

Questions?

Next Step Test Prep MCAT 2015 Resources

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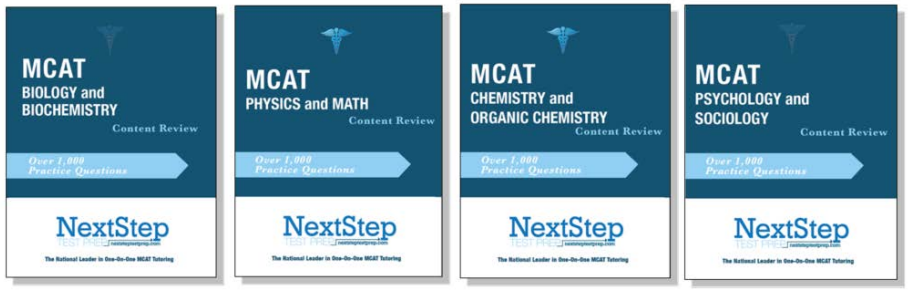

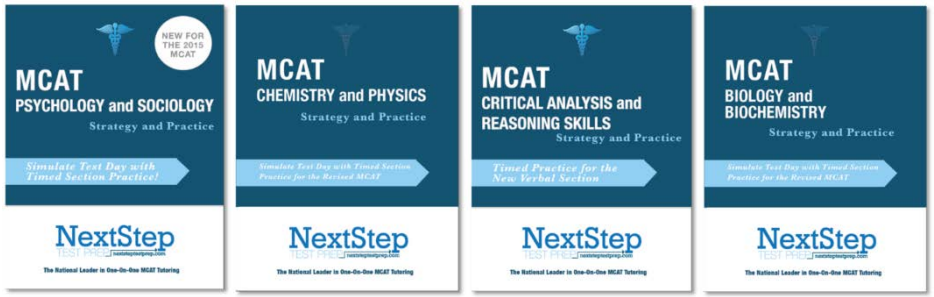

A few additional things….

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Critical Analysis and Reasoning Sample Class
Tuesday July 21st @ 8pm EST

Med School Selection and Application Strategies
Thursday August 6th @ 8:30pm EST

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Thank you for listening!

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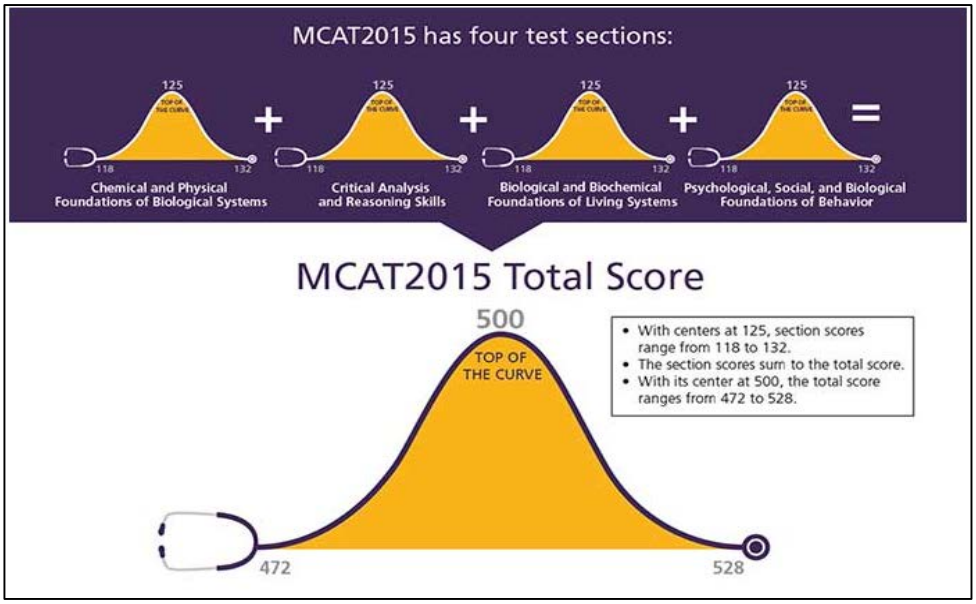
- The Critical Analysis and Reasoning Section is often the most challenging for pre-med students. This free video course provides an overview of strategies that will help you tackle this section of the test: **Click here to access this free video course!**
- **Click here** to sign up for our MCAT question of the day emails for great, free, practice content throughout the week.
- **Click here** for our MCAT blog.

Additional MCAT resources for sale from Next Step

- **Next Step's MCAT Book Store:** Next Step has published a nine book series to help students prepare for the new MCAT. These books are a great addition to any students MCAT library and we are unrivaled when it comes to prep for the verbal section of the new MCAT.
- **Next Step's Full Length Practice Tests:** Next Step has created 5 full length practice tests for the new MCAT.



MCAT 2015 Pre-Reqs Next Step Suggests:

Biology: 2 to 3 semesters
Chemistry: 2 semesters
O-Chem: 1 to 2 semesters
Physics: 2 semesters
Biochemistry: 1 semester
Psychology: 1 semester
Sociology: 1 semester
Statistics: 1 semester
Humanities: 1-3 semesters

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