Chemistry 2211a 2016 Final Exam preparation notes –

Questions and comments to consider – No need to answer all questions – just think about the points made

Chemistry 2211a – Metals in Life MJ Stillman

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Syllabus for Final Exam 2016.
Final Exam Preparation – Check the lectures and suggested web sites for answers to the questions

Syllabus for Final Exam

(Bring a calculator; no Periodic Table provided)

The Final Exam will be weighted approximately
25% first part of the term up to the 1st test;
and
75% lecture material since the term test.

The will be about 16 short T/F questions worth ¼ mark each based on the summary sheets I edited and provided you on owl from your summaries.

The Final Exam will comprise approximately 50 "usual" multiple choice questions plus the 16 T/F questions

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Questions + Answers – not all questions here have specific answers – in some cases you need to refer directly to the notes – also no need to answer everything – just use the statements to remind you about the topic.

Revision –r16-dE

FINAL EXAM REVIEW

LECTURE SECTIONS COVERED IN 2016

1. Introduction – background to essential – toxic metals and ligands
2. Important chemistry and special inorganic chemistry for bioinorganic chemistry
3. Biology and Biochemistry important for bioinorganic chemistry
4. Physical methods used to study metallobiolgical molecules –
5. The role of Mg in photosynthesis
6. The role of zinc (an essential group 12 metal)
7. Toxicity of metals: As - from the Introduction and through numerous examples, also Pb, Cd, Hg

GENERAL READINGS IN THE TEXT BOOKS:

Kaim..Klein - the new red book..

Ch 1 and 2 - good introductions
Ch 4 - Mg
Ch 17 for the metals I have mentioned
Ch 18/19 - metallodrugs and imaging - but you only need to know elements - we didn't include actual applications

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LIPPARD & BERG: (an old book - in the library - has a series of interesting sections.

1-10; sections: 1.3.d;-19; 21-26; (not sections 2.1.d – 2.2b); section 2.3; Qu. 1, p 40. Ch 3 – p 43-50; 56-66; section 3.3.b – a good summary of B12 – the difference between the vitamin and the cofactor is the replacement of CN- by adenosine;

Ch 5 – essential metals – p 103-115 (but be selective – just the material that follows the lectures – no CD data for example). Section 5.3.b applies to the Transport and Storage poster; p 131-133 (no Mo); Qu 1 (yes! The same as before).

Ch 10 257-275; (Mg-ATP on p 277 gives a good view of the Mg^{2+} interaction with ATP).

Section 12.2.c – good summary of the role of zinc.

TOPIC: INTRODUCTION
Major points to review:

1. **Metals and life**
2. **Critical or essential metals**
3. **Beneficial metals**
4. **Group 1 and 2**
5. **Alkali metals – Na, K - role**
6. **Alkaline earths – Mg, Ca**
7. **Charge/Size ratios important**
8. **Concentration gradients across cell membranes**
9. **Pump in K and Mg, pump out Na and Cl**
10. **Details of each Group 1 and 2 metal**
11. **Transition metals**
12. **Co, Ni, Cu (Wilson's disease; respiration), Zn – numerous enzymes – we studied 3**
13. **All are trace metals (except may be for Fe)**
14. **Key to know are Cr, Mn, Fe (v. imp – daily intake 10-15 mgs)**
15. **Toxic metals**
16. **Why toxic? Interactions possible? Chelators**
17. **Fe – various roles – transporters: transferrin; storage: ferritin; ferrochelatase**
18. **Fe in heme proteins**

Qu. What are the arguments used to support why mammals use the metals they do in their physiological chemistry?

4 essential metals are? 3 toxic metals are?

**I find the links at various times during the year – they might not all work this week. In that case, just move to the next one.

http://www.portfolio.mvm.ed.ac.uk/studentwebs/session2/group29/irontox.htm

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…from the notes –

What are metal complexes?
Identify a number of essential metals.
Identify toxic metals.
Answer the question – how are metals essential?
How are metals toxic?

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5) Copper is an essential metal – answer the questions:

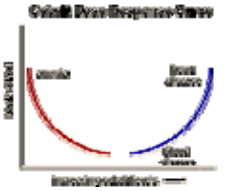
What are the oxidation states that copper adopts in the body?
What does copper do in the body? You may need to visit web sites.
What will you plan to do? Search out more copper-containing foods or eat fewer?

6) Review the information here – learn the role of the following metals – note they are the same as above:

Metals that we cannot live without are sodium (Na), potassium (K), magnesium (Mg), calcium (Ca), iron (Fe), cobalt (Co), copper (Cu), zinc (Zn)

Metal:	**Function:**
cobalt (Co)	core of Vit B_{12} (required to make blood cells)
copper (Cu)	part of redox enzymes used in defense against oxidative damage, for example superoxide dismutase (SOD)
sodium (Na)	important for extra cellular cations (positively charged ions or molecules) and nerve function
calcium (Ca)	part of bones; important for blood clotting
potassium (K)	major cation in intracellular fluids; essential for nerve and heart function
zinc (Zn)	part of dozens of enzymes; plays a role in reproduction and sexual maturation
iron (Fe)	found in hemoglobin and other enzymes

7) Explain the dose response for all metals.



As an example: Cobalt is an essential metal for humans. People who don't get enough cobalt in their diet have trouble making enough red blood cells. Cobalt is a component of vitamin B_{12} which helps in the process of making red blood cells. Without enough red blood cells, anemia develops. People with anemia experience symptoms of tiredness, weakness and listlessness. However, too much cobalt is also dangerous. When someone is exposed to too much cobalt, they may develop blood diseases and heart problems. Some people exposed to cobalt occupationally have developed lung disease and it may be linked to lung cancer.

8) Consider the following questions – explain briefly – so you would recognize the correct form the incorrect answers offered in a real quesiotn

Which of the following might exist? But which is NOT a normal function/role of metal in the body?

A. cobalt in the heme of hemoglobin
B. lead in bones
C. chromium in Vitamin B_{12}
D. phosphorus in ATP
E. arsenic in ATP

9) Which of the following is NOT characteristic of metals?

A. Metals are often charged ions.
B. Metals can be destroyed or degraded in the body.
C. Metals easily bond to other molecules.
D. Metals can have various oxidation states.

10) Some comments – consider these facts:

Metals are elements, so they cannot be destroyed or broken down. Metals can remain in the environment and in human bodies for long periods of time. Metals cannot be broken down to reduce toxicity but the speciation – that is – the form of the ligand molecules bound to the metals can havea

profound effect on toxicity. EG, ionic, trivalent arsenic can be made less toxic by the addition of a methyl (CH_3) group. For which metal is the biological toxicity exactly the opposite of this?

11) How does the size of an element change with its oxidation state? Oxidized? Reduced?

12) What controls the ability of a metal to form a complex with a ligand?

Background: Metals can have different species with different amounts of charge and these charged atoms easily and quickly form complexes with enzymes and other biological molecules. The amount of charge also affects how easily the metal can get into cells. Iron, for example, in the Fe(III) species, cannot cross membranes very easily. This restricts where it can go in the body. Hg can only easily penetrate membranes and be quickly distributed around the body if it is what form? Which form of Hg will not be so toxic to humans? Why not?

13) Who is LEAST likely to be exposed to toxic metals?

A. a technician working on a computer component board assembly line

B. a person who drinks water from a ground water well

C. a person smoking a cigarette

D. a person working on a new home computer

E. a painter renovating an 100 year old home

Background:

Metals can occur naturally

Metals occur in nature in rock formations, and are all around us in our environment. Most people are usually not exposed to metals, but sometimes, metal exposures do occur. For example, arsenic is sometimes found in drinking water that comes from a ground water source. It gets into the ground water by the normal process of leaching out of rocks and soil. Arsenic can be toxic to humans and is associated lung cancer and skin cancer.

Cadmium and human activities

Many metals exposures are due to human activities. For example, almost everyone is occasionally exposed to cigarette smoke and cigarette smoke contains cadmium, a potentially toxic metal. Cadmium is also found in lead and zinc ores. Symptoms of cadmium poisoning include nausea and vomiting, and if inhaled, lung lesions and chronic bronchitis.

Lead-based paint

Another common source of metals in our environment is old paint. Paint applied before 1973 is very likely to contain lead, a toxic metal. Old paint can often be 100% lead salt because the original organic solvents have evaporated, so chips of the paint are deadly to young children and dust can be inhaled by adults doing renovations. Lead poisoning in adults can result in a wide range of symptoms from weakness and loss of appetite to coma and death in very acute or massive exposures.

Metals in computers

The semiconductor industry uses many types of metals. Semiconductors are parts of personal computers. During the manufacturing process, toxic metals are often created as by products. There is no exposure from the use of the finished product.

Mercury in fish

Some people have been exposed to mercury in the fish that they eat. Many of the fish in the Great Lakes region of Canada and the United States are contaminated with methylmercury. People are often requested to limit their intake of fish from these lakes. Mercury was deposited in the lakes from air contaminated by the smokestacks of coal-burning power plants, waste incinerators, and factories, as well as from pulp and paper run-off. Bacteria in the lakes convert many forms of mercury into methylmercury, which can be concentrated in fish. Mercury is a "neurotoxin." It damages the brain and nervous system. Symptoms include weakness, fatigue, not being able to concentrate, headaches, tremors in the hands, and memory loss. Even more severe symptoms are possible.

14) Big ligands – enough of salts – covalently bound metals are important too

Nomenclature of Tetrapyrroles – that is the generic name of the chlorins, corrins, corroles, porphyrins

Chlorin

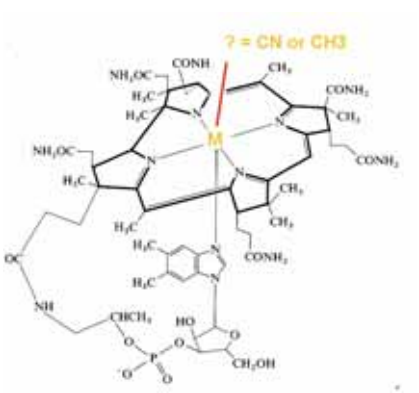
- notice how chlorin is not the same as protoporphyrin IX – takes a bit of searching for the very subtle changes – that means everything to the way chlorophyll works.

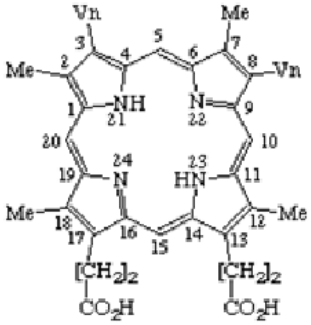
http://www.chem.qmul.ac.uk/iupac/tetrapyrrole/TP/E2.html
Chlorophyll *a* – **notice the R = phytyl chain – what is that?**

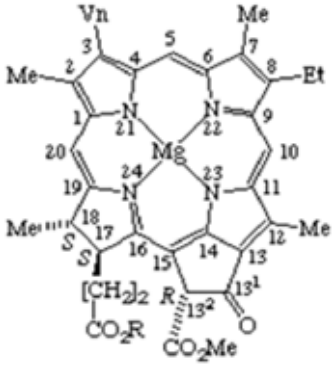
Cobalamin – the corrin ring

Protoporphyrin IX

15) Which metals typically bind in chlorophyll, corrin, and protoporphyrin IX in biology?







16) What is the difference between these 3 metals?

Calculations to try

Equilibrium:

1) Calculate K for $N_2 + 3H_2 \rightarrow 2NH_3$
if at equilibrium, $[N_2] = 1.03$ mol/L; $[H_2] = 1.62$ mol/L; and $[NH_3] = 0.102$ mol/L
(Ans K=0.00238)

2) $Br_2 + Cl_2 \rightarrow 2BrCl$
at 25 C, 1 atm pressure, $\Delta H = +29$ kJ/mol; $\Delta S = 105$ J /mol deg. Calculate ΔG for this reaction. (R=8.31 J /mol deg) T=298 K.
(Ans: -2)

3) Calculate $\log_{10}\beta_6$, β_6, $\Delta G^0{}_1$ and $\Delta S^0{}_1$ (that is for the 1st step) using these data:
$[Ni(H_20)_6]^{2+} + NH_3 \rightarrow [Ni(NH_3)(H_20)_5]^{2+} + NH_3 \rightarrow [Ni(NH_3)_2(H_20)_4]^{2+}$ etc to $[Ni(NH_3)_6]^{2+}$ in 6 steps with the following log K_n values:
n=1-6: 2.79, 2.26, 1.69, 1.25, 0.74, 0.03 at 303 K.
$\Delta H^0{}_1 = -16.8$ kJ/mol and R= 8.314 $JK^{-1}mol^{-1}$
(Ans: 8.76; 5.75×10^8; -16.2 kJ mol^{-1}; 1.98 $JK^{-1}mol^{-1}$)

TOPIC: INORGANIC CHEMISTRY - still included because is vital to the Metal Ions in Life topic…

Major points to review:

1) Metals in the Periodic Table
2) Know the d block metals - - know the electronic configurations of the 'key' biological metals – see p 2/3 of the unit
3) Know the common biological oxidation states of metals
4) How does size, matter for cations and anions?
5) Know donor atoms of ligands – these control the Hard/Intermediate/Soft nature of the ligand
6) So which metal matches up with which donor atom? And, where do you find those donor atoms, which ligand?
7) Ah, ha, soft, intermediate, hard – which metal is which? Which donor atom is which? Essential metals in biology
8) Ligands – know the names AND molecular structures of the important metal binding amino acids
9) And, the rings
10) How do the 3d orbitals split for Fe(II) and Fe(III)?
11) Redox properties of oxygen – see p 27 – the important oxygen species.
12) Read the 'Key Points' section
13) **Essential Metals**
14) Know an example of group 1 and 2
15) Know example charge/size rule
16) Know form concentrations in and out of cells – concept of pumps
17) Know what these metals do – simple examples
18) Transition Metals or d block metals (dbM)– important metals: Cr, Fe, Co, (not Ni) Cu, Zn, and the triad Zn , Cd, Hg

Make sure you have learnt the location in the Periodic Table of: Na, Mg, K, Ca, and the d block metals we've discussed or are part of posters.

QUESTIONS

1. What is oxidation - reduction? Why is it so important in biology? Give examples – yes several – where an electron is added to a compound or element

in a compound – and another where an electron is removed from a compound. All from the notes.
2. What are metals? Why are metals so prevalent in the environment today?
3. What are the electronic configurations of the 12 key elements
4. Book work
5. How are d orbitals different from p orbitals?
6. What are ligands? How can you define the chemical property of a ligand?
7. Donor atoms are selective for similar types of metal – what is this property?
8. Which metals are hard? Which donor atoms are hard?
9. Name 4 hard metals, 4 soft metals, 4 intermediate metals, 4 hard ligands, 2 soft ligands, 2 intermediate ligands
10. Draw three amino acids that are intermediate or hard ligands.
11. Is ATP a hard, Intermediate or soft ligand?
12. Identify 3 important natural rings in biology
13. Name the 5 important oxygen species in biology
14. What is BAL? What was Lewisite?
15. What are essential metals?
16. Are all metals essential?
17. Are all metals toxic?
18. How would you compare essential/beneficial metals to 'toxic metals'?
19. Is this a fair comparison?
20. Is it Black and White?
21. How many metals are essential? Have no known use? Are toxic?
22. Is it clear-cut which metals are toxic?
23. How can you define an a metal as essential – see url 3 above
24. Iron is essential – how much is best? Is 'too much' possible?
25. Chromium is essential – in all oxidation states?
26. Are essential metals always present in mg/kg quantities in the average human body?
27. Are roles for all metals known?
28. Are all essential metals now known?
29. Can an essential metal become toxic? Give examples.
30. Why do we need metals anyway?
31. And, what about human health – how many do we require?
32. Do the questions on p 31 and 32 of the INORG unit
33. The common oxidation states (numbers) of Na, K, Mg, Ca, Cr, Fe, Co, Cu, Zn, Cd, Hg, Pb, As are:
34. Name three electropositive elements
35. Name three electronegative elements
36. What are the donor atoms in desferrioxamine B? How many bind the metal? For that matter – which is the metal targeted? Why do you thin this metals AND its oxidation state bind to Desferrioxamine?
37. What is the shape called?
38. What is this chelator used for?
39. What is a ligand?
40. Name a good hard ligand molecule
41. EDTA is what? Draw its structure
42. How does it bind to metals? What is it used for in medicine?
43. Name three hard amino acids
44. Name a good soft ligand
45. Name 1 soft amino acid
46. Which amino acids does Zn bind to usually?
47. And K+?
48. And Ca2+?
49. What does it mean when we say the Ksp for HgI_2 is 10^{-30} ?
50. And Ksp for HgS is 10^{-53} ? Calculate the free Hg^{2+} concentration at equilibrium assuming pH 7 and no other ions are present.
51.
52. Calculate β_4 for the reaction in which Cd^{2+} + GSH => => => $[Cd(GSH)_4]^{2-}$
53.
54. For which K1= 108; K2= 108; K3= 109; K4= 1010;
55.
56. What is the difference between Kn (n=1, 2,3) and βn (n=3)?
57.
58. What is the chelate effect in this context?
59. What controls the value of β for EDTA4- binding to a metal?

TOPIC: Biology needed for BioInorganic Chemistry
Major points to review:

1. Amino acids
2. Proteins – peptide bond
3. Nonenzymatic proteins; enzymes
4. Special absorption spectral properties of amino acids
5. Aromatic amino acids
6. Protein structure – peptide bond
7. How proteins are made – tRNA codes for each amino acid
8. Folding – primary, secondary, tertiary and quaternary structures
9. Nucleic acids: DNA and RNA – the purines and pyrimidines

10. How the DNA chain is formed – tying bases to the sugar phosphate chain
11. (Need to be able to draw the 4 DNA bases, adenine, guanine, cytosine, thymine; know which form pairs: TA & CG; be able to draw the sugar phosphate backbone – see 27th Oct lecture – and attach a base)
12. Know an example of basic, acidic, aromatic amino acid
13. Know example of N- binding; S- binding; $-O^-$ binding amino acids
14. Know form of peptide bond
15. Know about the absorption spectrum of aromatic amino acids
16. Know how proteins are synthesized using RNA in vivo
17. Know the 4 structural features of proteins
18. DNA
19. Know the 4 DNA bases
20. Know how they bind using hydrogen bonding - see the course outline above

QUESTIONS

21. Which amino acids are important for metal binding?
22. What are structures of these amino acids?
23. What are the donor atoms? Are they hard, intermediate or soft?
24. How do amino acids form a peptide chain?
25. The peptide bond is special, why?
26. What is the template for protein synthesis?
27. How is the peptide chain lengthened?
28. What does crosslinking mean?
29. Which amino acids are likely to bind to metals?
30. How is protein structure defined? Describe the different structural features.
31. How do the heme proteins myoglobin and hemoglobin fold?
32. Where about (wavelength range) do aromatic amino acids absorb in the UV-visible spectrum
33. WRT to protein structure - What is hemoglobin a good example of?
34.
35. Iron, Copper, and Zinc are examples of cofactor – what are the proteins associated with these metals? (Mn and Mo are not part of the Final Exam)
36. Be able to recognize the important rings – be able to draw PPIX
37. What does denaturation mean? How can it be observed? Is it reversible?
38. Know that this is 7.3 kcal/phosphate (p 19)
39.
40. How does Mg2+ become involved in ATP etc.?
41. What is the structure of the polynucleotide chain?
42. What is the structure of the 4 bases? Be able to recognize them – if provided with the structures and the know the pairing and the number of hydrogen bonds formed (2 for AT vs 3 for CG)
43.
44. Know there is a major/minor groove - rise per turn (5.4 A)
45.
46. Be able to draw the polynucleotide chain showing where the bases are located – this means be able to identify a correct sugar-phosphate backbone see p 20
47. Where does protein formation take place in the cell?
48.
49. What is the structure of lipids – 3 types, sat/unsat/polyunsat (which is one your instructor should eat, NOT eat?)
50. Know that all sorts of chemistry take place through the membrane
51.
52. Structure of prokaryotes vs eukaryote cells – which are typical of mammals?

TOPIC: Instrumentation –

Use the following to answer the questions about biological purification: (use the TextSelect tool to copy the url to the ClipBoard then paste into your browser)
http://www.forumsci.co.il/HPLC/program.html
http://www.hopkinsmedicine.org/mams/MS2004%20Lecture%204%20-%20Chromatography.pdf
http://www.forumsci.co.il/HPLC/HPLC_overview_handouts2002.pdf

Know how liquid chromatography works: SEC and HPLC
Know how AAS works to measure metal concentrations

QUESTIONS – part 1

1. How does the HPLC work?
2.
3. How does the packing in size exclusion (gel permeation) chromatography help protein purification/protein separation?
4. Why do the analytes applied to a column separate?
5. What does the coating do in HPLC? What is it often?
6.
7. What is the order of elution from a size exclusion column? Why?
8.
9. How can an unknown be determined? What do the standards help with?
10.

11. Why is it a good idea to reduce the band width (or reduce band broadening)?
12.
13. Use the following to answer the questions about measurement of metal concentrations:
14.
15. http://www.resonancepub.com/atomicspec.htm
16. http://www.chemistry.org/portal/a/c/s/1/feature_tea.html?id=c373e9fc5e4e9a828f6a4fd8fe800100
17. http://ull.chemistry.uakron.edu/analytical/Atomic_spec/
18. http://elchem.kaist.ac.kr/vt/chem-ed/courses/spec/atomic/theory.htm
19. http://elchem.kaist.ac.kr/vt/chem-ed/spec/atomic/aa.htm Check the atomic absorption questions-duplicated below
20.
21. QUESTIONS – part 2
22.
23. What is the form of the metal when it is sucked into the nedulizer? For that matter, what happens before the nebulizer? What is the nebulizer? Why does the AAS instrument need a nebulizer?
24.
25. What is actually measured in AAS?
26.
27. What is measured in AES?
28.
29. What does the hollow cathode lamp do?
30. What are the common gases used to make the flame?
31.
32. What is the common temperature range of the flame?
33. What happens to the sample in the flame
34.
35. Why is it necessary to observe at a specific height above the burner?
36.
37. How are concentrations determined by this method?
38. What is the Beer-Lambert law? Why can it be used in AAS?
39. What are the common concentration units used in AAS and AES?
40. What are the common ranges for most metals?

TOPIC: Mg

Major points to review - taken from the unit

24 g in the 70 kg man. About 90% is in bone and muscle (meq?). Meaning? Deficiency is rare in adults - alcoholism, burns, renal disease, cirrhosis of the liver, cardiovascular disorders. Mg deficiency can result in disastrous consequences - seizures, coma, death Excess leads to anesthesia - ie a coma-like condition

The role of Mg in mammals is widespread and includes not only a role in activating many enzymes, particularly phosphorylation Ca/Mg-ATPases, Also, heart disease in hard-water areas (eg London, UK) much less than in soft-water areas (Glasgow, UK).

Conversion of solar energy into a synthetic organic driving force – once the first reaction occurred; there was no going back – why not?

All photons absorbed between 400 and 700 nm can run photosynthesis. But all are used at energy equivalent of a red 660 nm photon. (Why? Remember the energy level diagram from INSTR unit).

Plastocyanin (Pc) is a small (10.5 kDa) Cu-containing protein which acts as an electron carrier between the cytochrome b_6f and photosystem 1 (PS1) complexes in the photosynthetic electron-transfer chain. Pc belongs to the group of so called type 1 copper proteins which are characterized by a strong blue color. 2^0 and 3^0 structure is? β pleated sheet.

The copper(II) d^9 ion near the top is coordinated in an approx. tetrahedral symmetry by His-37, Cys-84, His-87 and Met-92.(N, SH, N, CSC)Cu flips 1+ to 2+ and back $Cu^{2+}Pc + e^- \rightarrow Cu^{+}Pc$

Why does this work - what colour do you predict Pc is when reduced?

The scheme below summarizes the overall reaction catalyzed by PSII

$$2H_2O + 2PQ \xrightarrow{\text{LIGHT/Chlorophyll PSII}} O_2 + 2PQ(2H) \text{ or } PQH_2$$

PSI: Photosystem I the primary electron donor is P700. Accepts electrons from a bound (PC) plastocyanin. Reduces (Fd) ferredoxin, an Fe/S (this time Fe_4S_4) protein.

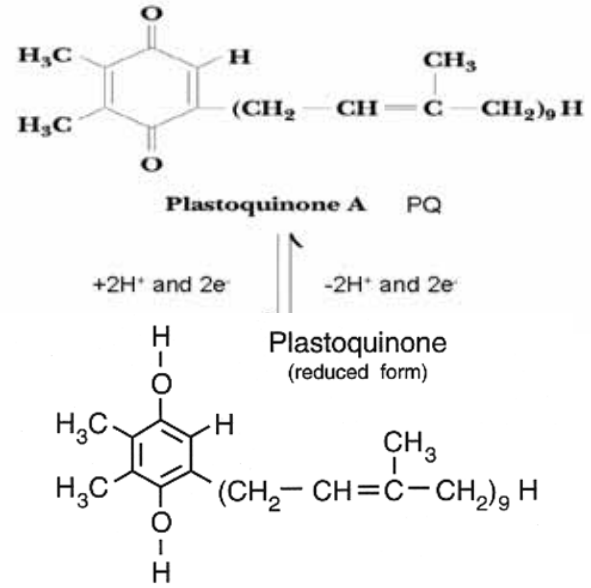
NADP+ is reduced to NADPH from ferredoxin by ferredoxin-NADP+ oxidoreductase.

The chemical balance summary is very important
Light driven reactions:
12 NADP+ + 18 ADP + 18 P + 6 H^+ + 48 hv (photons) → → $6O_2$ + 12 NADPH + 18 ATP + $6H_2O$

The Calvin reaction is:
$6CO2 + 12NADPH + 18ATP + 12H_2O \rightarrow \rightarrow \rightarrow C_6H_{12}O_6 + 12NADP+ + 18ADP + 18Pi + 6H^+$ notice imbalance of NADP and ATP 12:18.

Plastoquinone PQ is:

PQ molecule and reaction



1. Why are the structural components in the leaf so important to photosynthesis?
2.
3. At what point do we have: H_2O split to evolve O_2 and NADPH synthesized?
4. ADP + P_i → ATP + H_2O (is an endergonic reaction (why obviously?) - needs energy from the proton gradient).
5. Where is the proton gradient coming from? Tthe H^+ set up a gradient – that gradient = a voltage – a driving force across the membrane.
6. Nicotinamide adenine dinucleotide (NAD) consists of two ribose rings, one with adenine attached to its 1' carbon atom and the other with nicotinamide at this position; these two sugar-heterocycle moieties are joined together by a bridge of two phosphate groups through the 5' carbons. In $NADP^+$, the ribose ring attached to the adenine has an additional phosphate group at the 2' position.

TOPIC: Zinc
Major points to review:

1. Zinc is a major part of enzymes
2. Zn binds to certain amino acids – hard, intermediate and soft donor atoms
3. Catalysis often is due to polarization of H_2O or COOH bonds
4. Need to look at the different structures adopted
5. We studied in details CA, CPA and ADH
6. Metallothionein is a key Zn and Cd binding protein – not an enzyme
7. Zn finger proteins use 4 CYS so Zn is structural
8. Dietary Zn important – excess hard to achieve
9. Usual terrestrial distribution – aided by man's activities
10. CA – key is the activation of CO_2 by polarized water
11. CPA – attack of the peptide bond by polarized activated water is the key plus the hydrogen bonds
12. Liver ADH – 2 cycles needed – NAD+ and the alcohol
13. Zn finger proteins can contain many different loops and therefore a number of Zn atoms are required.

QUESTIONS

1. What are the common ligands for Zn in biological systems? The donor atoms? The amino acids? The molecules?
2. Name 5 different Zn-containing proteins or enzymes
3.
4. What is Zn essential for in mammals?
5. What does deficiency result in?
6.
7. Under what conditions is severe deficiency found in humans?
8. What is special about metallothionein?
9.
10. What are the ligands in metallothionein?
11. What is the reaction catalysed by CA?
12. What are the ligands for Zn in CA?
13. What is the effect of pH on CA activity? Why is this the case?
14. What is the key reaction that Zn is involved with in CA?
15. What is a protease?
16. Why do we need them?
17. How is the Zn bound in CPA?
18. What is the key feature of this reaction? What makes it work?
19.
20. What is the role of water in this reaction?
21. What do the hydrogen bonds do in CPA?
22. How many Zn are there in liver alcohol dehydrogenase? LADH

23. What are the ligands in the binding site(s) of the Zn(s) in LADH?
24. Why is there a difference? How does the difference relate to the function of LADH?
25. What is the actual reaction catalysed?
26. Is there a 2nd reaction?
27. What is NADH? Why is is involved with LADH?
28. Without using formula – describe the oxidation/reduction reaction of NADH

TOPIC: Toxic Metals

Major points to review:

Know where in the Periodic Table all the key toxic metals are located – know if they are soft, intermediate or hard metals.

1. Toxicity depends on speciation – know what changes the speciation – know what increases solubility - very important to know the species that is most toxic
2. Know key metals
3. Know example of mercury – speciation – toxicity – where - when
4. Know cadmium, lead and arsenic
5. Mercury – cations vs methylated forms; Minamata Disease – what, why, where, when, where else
6. Cadmium – only cations – itai itai disease
7. Arsenic - - 3+ vs 5+; drinking water; protecting wood in the ground
8. Lead
9. Chelators – what are they, what are their formulae, what are their names, how do they work, describe which used for which metal(s) – be able to recognize the molecules (p 6)
10. Know routes of exposure and toxic response – acute vs chronic
11. Poisoning in … - not included in the exam.
12. Know the details of the metals, first the summary: – 1) lead – the yellow highlighting are the key points – 2) cadmium, 3) arsenic, 4) mercury – see the banners for key points about Hg.
13. Chelators – as before – now with metals connected – know top 2 chelators for each metal (Pb, Cd, As, Hg).
14. Where do toxic effects occur?
15. Use the following to answer the questions about toxic metals (please note that I accumulate these sites over time and some may not work - I do not use the content for exams - these are for your greater background)

http://www.oralchelation.net/data/ToxicMetals/data13b.htm - menu of short paragraphs of information on many topics
http://www.iupac.org/publications/pac/2002/pdf/7405x0793.pdf
http://www.biologi.sdu.dk/gb/research_groups/ecotox/gruppe.htm - good overview
http://www.dartmouth.edu/~toxmetal/TXSHhg.shtml
http://www.lehigh.edu/~kaf3/books/reporting/hvymtl.html
http://www.osha.gov/SLTC/metalsheavy/index.html
http://www.osha.gov/SLTC/mercury/
http://www.osha.gov/SLTC/cadmium/index.html

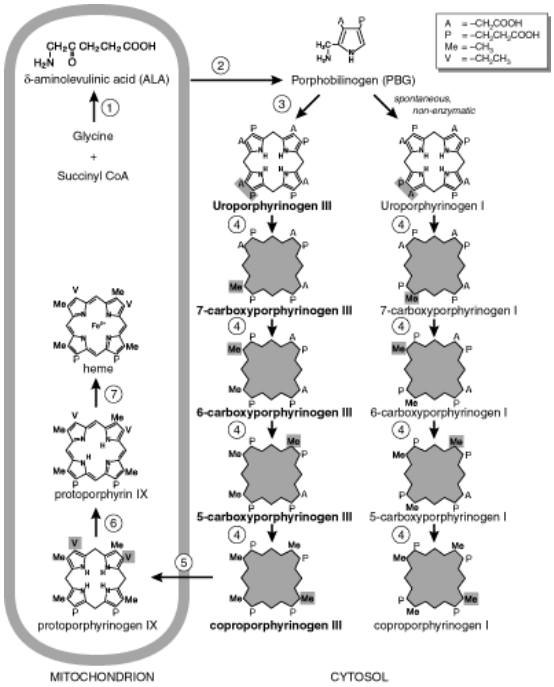
http://www.mercola.com/2003/dec/27/toxic_metals.htm
http://millennium-debate.org/ind18march3.htm
http://www.generationgreen.org/metals%20overview.htm
http://www.cqs.com/toxicmetals.htm
http://www.oralchelation.net/data/ToxicMetals/data13b.htm#7 - very short
http://www.oralchelation.net/data/ToxicMetals/data13b.htm#20
http://www.toronto.ca/health/factsheet_ptw.htm As – CCA
http://www.epa.gov/oppad001/reregistration/cca/
http://www.caes.state.ct.us/PlantScienceDay/1999PSD/arsenic99.htm

QUESTIONS – Note – there are large number of comments and questions at the end of the TOXIC METALS unit as well as here

1. What are toxic metals?
2. Which metals are very toxic?
3. Which are the 4 or 5 most toxic metals? And, where are humans exposed to them, and what is the overall effect of this exposure?
4. What is the Bertrand diagram? What does it tell us?
5. What sort of diseases do toxic metals cause?
6. Is there any difference in the site of the toxicity for each metal or do they all cause the same sort of damage?
7. Which toxic metals commonly found around the home?
8. Why are many toxic metals classified as intermediate or soft?
9. What are the primary exposure routes for humans?
10. What does acute and chronic mean wrt to toxicity?
11. Why are the kidneys and liver prime sites for damage from most toxic metals?
12. What does LD50 mean? General knowledge
13. How do metals enter the cell? Name the 4 routes
14. Why is crossing the blood brain barrier so often referred to when speaking of mercury?
15. Why did the Romans have an issue with Pb?
16. How is heme synthesis related to the presence of Pb?

17. As a follow up – think what you could do in your daily life to reduce lead exposure. OR how to protect yourself against lead & other metal poisoning
18. What does exposure to Pb result in for children?
19. Is Pb as deadly in adults?
20. How does Pb lead to anemia?
21. How has a change in gasoline been mirrored in the humans?
22. Where is Pb used in products?
23. Where is Pb likely an exposure risk to humans?
24. What is the role of D-ala in Pb poisoning?

ANS-Pb blocks ALA synthetase so that dALA builds up and heme is not made



1. How is Pb measured in humans?
2. About what is the Pb exposure level that results in damage to children?
3. Why are ducks at risk from Pb poisoning?
4. How is mercury released into the environment?
5. How does mercury affect health of humans?
6. What are the conditions toxic metals become a concern?
7. What cases of poisoning by toxic metals are well known? Which metals?
8. Why do acidic fruit drinks pose a hazard?
9. How is cadmium different from mercury in its toxicity?
10. Why is cadmium a problem in the workforce?
11. Is cadmium a problem in the home?
12. Why is dental amalgam considered potentially dangerous?
13. What is the concern with some vaccine solutions?
14. Are there restrictions on the consumption of fish? Why?
15. Why is smoking so dangerous (other than nicotine and lung cancer)?
16. Why are computers a problem?
17. Where in the world is mercury a current problem?
18. Are there any elements/compounds that protect mammals from the effects of toxic metals? What are they?
19. What makes a metal toxic?
20. Is it easy to identify a toxic metal?
21. Which metals are absolutely toxic?
22. Which metals may be essential at some concentration?
23. Which metals are always non-toxic?
24. Which As compounds are not toxic?
25. A major recent concern from As poisoning has been the chemicals used for pressure-treating wood:
26. How are people exposed to arsenic?

1. Why is pressure treated wood such a problem?
2. How significant is the health risk posed by CCA-treated wood?
3. CCA= chromate copper arsenate – dyed green
4. What are currently considered the best methods of making a CCA lumber surface safe from arsenic exposure?
5. How can I minimize arsenic exposure if my child plays on CCA lumber?
6. Can I use CCA-treated wood in fireplaces? In a wood-burning stove?
7. What precautions should I take when handling CCA wood?

8. What about arsenic contamination of the soil or sand under and around CCA wood structures?
9. What should I do if CCA wood is in or near my garden?
10. How long does CCA lumber continue to be an arsenic exposure hazard? Does risk go down over time?
11. Is there any way to look at CCA lumber surfaces and tell how much arsenic might come off from hand contact?
12. What was Lewisite? Where was it used? What is BAL?
13. What is the concern with As and water?
14. Where does the As come from in water?
15. How many people are affected? Roughly.
16. What are the major symptoms of chronic As poisoning?
17. What is glutathione? How does it bind to As?
18. Where in the world are the worst outbreaks of As poisoning today?
19. Is As a concern only there?
20. What causes the As to be released into the water?
21. What is the concern with Cd?
22. Does Cd poison like Hg?
23. Is Cd short lived in the body?
24. What is the major disease caused by Cd?
25. Where is Cd used in products?
26. What are the target organs for Cd damage?
27. Where does Cd enter the environment from? How are we exposed to Cd?
28. What is metallothionein's role in Cd metabolism?
29. What happened in Japan wrt Cd?
30. How many toxic forms of Hg are there?
31. Have there been instances of Hg poisoning world wide?
32. Why?
33. In Canada? Why?
34. What are the exposure routes for man?
35. Where is Hg used in products?
36. Where are we most usually exposed to Hg?
37. What are the health effects of Hg exposure? Are there differences depending on the form?
38. How does glutathione become involved with Hg?
39. Why is Hg^0 so dangerous?
40. Where is the target organ for methyl mercury?
41. Where are we exposed to methylmercury?
42. What detoxifying agent that could be used?
43. Where do fish and shellfish enter into the Hg story?
44. How? Why?
45. Is exposure the Hg fast acting or slow?
46. Can hair be used to assess Hg exposure?
47. What happened in Minamata? When? Where?
48. When was the case closed?
49. Are the statements in this url all correct?
50. http://www.world-action.co.uk/poisoning.html
51. Critical questions to consider:

a. Is it safe to allow effluent from a city (storm sewer) or industrial plants to flow into a river – assuming that a small amount of any metal will probably precipitate and mix with the sediment – or be diluted to such a low concentration that it can't harm any organism?

b. Discharge of toxic metals is prohibited in Canada - but Hg(II) and $HgCH3^+$ is still a problem from Pulp & Paper mills. Pb arises from wrecking yards.

c. Comment on this report from the USA - : "For years, the EPA and the Army Corps of Engineers have maintained the discharges into the Potomac have no effect on the river or its aquatic life, including the short-nose sturgeon. One discharge is released through the C&O National Historic Park.. Preliminary analysis of sludge being dumped into the Potomac River by the Army Corps of Engineers shows high levels of arsenic, lead, mercury chromium, copper, zinc, nickel and selenium. " BUT also consider the statement from the manager: The arsenic discharges are one to two parts per billion in raw water, the aqueduct manager said. He would not address the other elements until he could review the laboratory findings, but said they should be present only in nondetectable or trivial amounts. What is your opinion? What would you do?

52. Are there different effects depending on the dose of a toxic metal?
53. How dangerous is mercury?
54. Are we exposed to Hg routinely in our daily lives?
55. Are the fish safe to eat?
56. What is the problem with rivers in Ontario? Explain the origins of the Hg in rivers.
57. Why is this Hg so deadly? What happens next, how?

58. And, where in medicine do we become exposed to Hg?
59. How is heme synthesis related to the presence of Pb?
60. See above
61. Qu. As a follow up – think what you could do in your daily life to reduce lead exposure.

63. How is it applied?
64. How does it work?
65. What makes a 'perfect' chelator?
66. What are the molecules used commonly today?
67. Can you draw their structures?
68. What is a common theme between the chelating molecules and the metals they chelate?

CHELATION THERAPY AND CHELATORS

62. What is chelation therapy?

Chelating Agent	Toxin	Route**	Drug
Dimercaprol (BAL) (SH-SH)	Arsenic Lead Mercury (inorganic)*	i.m.	Dimercaptol Injection B.P. BAL in Oil
Dimercaptosiccinic acid (DMSA) (Succimer) (SH-SH)	Arsenic Lead Mercury	p.o.	Chemet
Dimercaptopropane- sulfonate (DMPS) (SH-SH)	Arsenic	p.o. i.m.	Bulk form (for compounding by pharmacists)
D-pencillamine (SH-NH2)	Arsenic Mercury Lead	p.o.	Metalcaptase Pencillamine Cuprimine Depen
Ethylenediamintetra- acetic acid (EDTA) (Edetate disodium)	Lead	IV	Chealamide Versenate

(O/O/N O/O/N = 6)

*Not methylmercury poisoning.

Source: Data from Beers et al. 1999; Micromedex 1999; Roberts 1999; Wentz 2000; Anon. 2001; Ferner 2001; Marcus 2001; USNML/NIH Drug Information 2001a; 2001b; 2001c; 2001d.