Chemistry 2211a – Bioinorganic Chemistry MJ Stillman

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

Syllabus for Final Exam 2018 (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; - MAINLY PERIODIC TABLE – electronic configurations but also amino acids
75% lecture material since the term test.

The Final Exam will comprise a mix of multiple choice questions, short answer questions and written answers.

FINAL EXAM REVIEW TOPICS see topic questions after the Term Test after about line 420

LECTURE SECTIONS COVERED IN 2018

Introduction – background to essential – toxic metals and ligands
Important chemistry and special inorganic chemistry for bioinorganic chemistry
Biology and Biochemistry important for bioinorganic chemistry
Biologically important ligands that coordinate metals
TERM TEST
The role of zinc (an essential group 12 metal)
Toxicity of metals: As, Pb, Cd, Hg
Mg in chlorophyll

TOPIC: INTRODUCTION

Major points to review:

Metals and life
Critical or essential metals
Beneficial metals
Group 1 and 2
Alkali metals – Na, K - role
Alkaline earths – Mg, Ca
Charge/Size ratios important
Concentration gradients across cell membranes
Pump in K and Mg, pump out Na and Cl

Details of each Group 1 and 2 metal
Transition metals
Co, Ni, Cu (Wilson's disease; respiration), Zn – numerous enzymes – we studied 3
All are trace metals (except may be for Fe)
Key to know are Cr, Mn, Fe (v. imp – daily intake 10-15 mgs)
Toxic metals
Why toxic? Interactions possible? Chelators
Fe – various roles – transporters: transferrin; storage: ferritin; ferrochelatase
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?

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

Are all essential metals nontoxic to babies and young people?

What are the oxidation states that copper adopts in the body?

What does copper do in the body? You may need to visit other sites.
Is the text correct do you think about how copper assists in biological functions?
What is the recommended intake of copper? Is this controversial?
Is there any indication that we over- or under- ingest copper?

What will you plan to do? Search out more copper-containing foods or eat fewer?

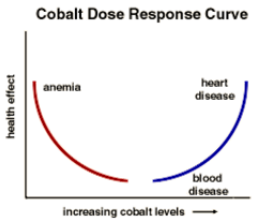
6) Review the information here – learn the role of the following metals – note they are the same as above:

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. This is the Bertrand Diagram turned upside down

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.



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8) Consider the following questions – research using the web sites above

Which of the following is NOT a normal function/role of metal in the body?

A. iron in the heme of hemoglobin

B. calcium in bones

C. cobalt 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 have a 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 the metal change with its oxidation state?

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

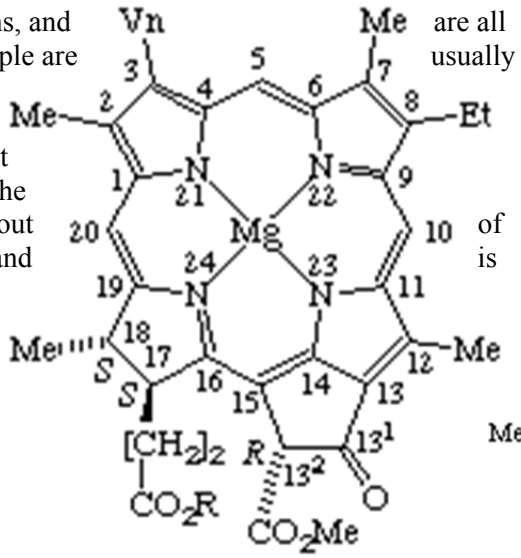
D. a person working on a new home computer

E. a painter renovating an 100 year old home

Background:

Metals can occur naturally

Metals occur in nature in rock formations, and around us in our environment. Most people are 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 rocks and soil. Arsenic can be toxic to humans and associated lung cancer and skin cancer.



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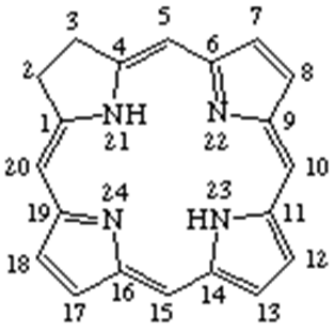
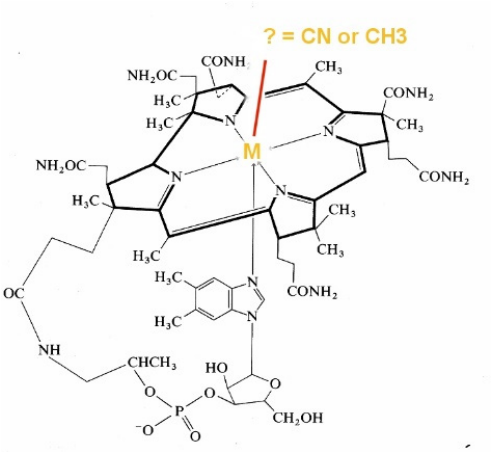
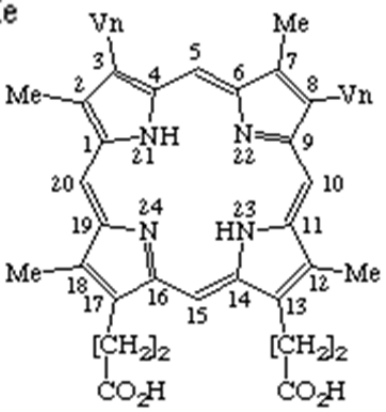






110 ## Cadmium and human activities

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.

111 ## 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.

112 ## 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.

113 ## 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.

114

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

116

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

Chlorin

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

Chlorophyll *a* – **notice the R = phytol chain – what is that? Be able to draw chlorophyll with its peripheral decoration but not the chain!**

Cobalamin – the corrin ring you do not need to draw cobalamin but be able to select it from a set of others

Protoporphyrin IX need to be able to draw and as heme add the Fe!

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
(=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.
(-2)

3) Calculate $\log_{10}\beta_6$, β_6, ΔG^0_1 and ΔS^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 $JK^{-1}mol^{-1}$
(8.76; 5.75×10^8; -16.2 kJ mol^{-1}; 1.98 $JK^{-1}mol^{-1}$)

TOPIC: INORGANIC CHEMISTRY

Major points to review:

- Metals in the Periodic Table
- Know the d block metals - - know the electronic configurations of the 'key' biological metals – see p 2/3 of the unit
- Complete the table on p 3
- Know the orbital shapes
- Know why the CO and O_2 bend when bound to the Fe(II) in the heme
- Ionization controls the electropositive / electronegative nature of all elements
- Know the common biological oxidation states – see the table on p 6
- How does size, matter for cations and anions?
- Know donor atoms of ligands – these control the Hard/Intermediate/Soft nature of the ligand – see p 9
- So which metal matches up with which donor atom? And, where do you find those donor atoms, which ligand?

Ah, ha, soft, intermediate, hard – which metal is which? Which donor atom is which? Know Table 2 on p. 10.
Essential metals in biology
Ligands – know the names AND molecular structures of the important metal binding amino acids – p 13
And, the rings on p 14-22
How do the 3d orbitals split for Fe(II) and Fe(III)? – see p 25
Redox properties of oxygen – see p 27 – the important oxygen species.
Read the 'Key Points' section, p 29 to end.

Essential Metals

Know an example of group 1 and 2
Know example charge/size rule
Know form concentrations in and out of cells – concept of pumps
Know what these metals do – simple examples
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

What is oxidation - reduction? Why is it so important in biology?
What are metals? Why are metals so prevalent in the environment today?
What are the electronic configurations of the 12 key elements?
How are d orbitals different from p orbitals?
What are ligands? How can you define the chemical property of a ligand?
Donor atoms are selective for similar types of metal – what is this property?
Which metals are hard? Which donor atoms are hard?
Name 4 hard metals, 4 soft metals, 4 intermediate metals, 4 hard ligands, 2 soft ligands, 2 intermediate ligands
Draw three amino acids that are intermediate or hard ligands.
Is ATP a hard, Intermediate or soft ligand?
Identify 3 important natural rings in biology
Why do the electrons pair up in 'high field splitting'?
When does this happen with myoglobin and hemoglobin?
Name the 5 important oxygen species in biology
What is BAL? What was Lewisite? Name the compound –
What are essential metals?
Are all metals essential?
Are all metals toxic?
How would you compare essential/beneficial metals to 'toxic metals'?
Is this a fair comparison?
Is it Black and White?
How many metals are essential? Have no known use? Are toxic?
Is it clear-cut which metals are toxic?
How can you define an a metal as essential – see url 3 above

Iron is essential – how much is best? Is 'too much' possible?
Chromium is essential – in all oxidation states?
Are essential metals always present in mg/kg quantities in the average human body?
Are roles for all metals known?
Are all essential metals now known?
Can an essential metal become toxic? Give examples.
Why do we need metals anyway?
And, what about human health – how many do we require?

Points to consider from the written notes from the overhead starting from September – Calculate the mass of CH_3HgCl in a 10 mL cell culture sample (assume = 10 g) for 0.06 ppb concentration of the Hg.

The common oxidation states (numbers) of Na, K, Mg, Ca, Cr, Fe, Co, Cu, Zn, Cd, Hg, Pb, As are: _____

Name three electropositive elements

Name three electronegative elements

What are the donor atoms in desferrioxamine B? How many bind the metal?

For that matter – which is the metal targeted? Why do you think this metal AND its oxidation state bind to Desferrioxamine?

What is the shape called?
What is this chelator used for?
What is a ligand?
Name a good hard ligand molecule

EDTA is what? Draw its structure

How does it bind to metals? What is it used for in medicine?
Name three hard amino acids

Name a good soft ligand
Name 1 soft amino acid
Which amino acids does Zn bind to usually?

K?
Ca?
What does K_{sp} describe?

What does it mean when we say the K_{sp} for HgI_2 is 10^{-30} ?
And K_{sp} for HgS is 10^{-53} ? Calculate the free Hg^{2+} concentration at equilibrium assuming pH 7 and no other ions are present.

Calculate β_4 for the reaction in which $Cd^{2+} + GSH \Rightarrow \Rightarrow \Rightarrow [Cd(GSH)_4]^{2-}$
For which $K_1 = 10^8$; $K_2 = 10^8$; $K_3 = 10^9$; $K_4 = 10^{10}$;
What is the difference between K_n and β_n ?
What is the chelate effect in this context?
What controls the value of β for $EDTA^{4-}$ binding to a metal?

TOPIC: Biology needed for BioInorganic Chemistry

Major points to review:

Amino acids
Proteins – peptide bond
Nonenzymatic proteins; enzymes
Special absorption spectral properties of amino acids
Aromatic amino acids
Protein structure – peptide bond
How proteins are made – tRNA codes for each amino acid
Folding – primary, secondary, tertiary and quaternary structures
Nucleic acids: DNA and RNA – the purines and pyrimidines
How the DNA chain is formed – tying bases to the sugar phosphate chain
(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)

Know an example of basic, acidic, aromatic amino acid
Know example of N- binding; S- binding; $-O^-$ binding amino acids
Know form of peptide bond
Know about the absorption spectrum of aromatic amino acids
Know how proteins are synthesized using RNA in vivo
Know the 4 structural features of proteins
DNA
Know the 4 DNA bases
Know how they bind using hydrogen bonding - see the course outline above

QUESTIONS

Which amino acids are important for metal binding?
What are structures of these amino acids?
What are the donor atoms? Are they hard, intermediate or soft?
How do amino acids form a peptide chain?
The peptide bond is special, why?
What is the template for protein synthesis?
How is the peptide chain lengthened?

What does crosslinking mean?
Which amino acids are likely to bind to metals?
How is protein structure defined? Describe the different structural features.
How do the heme proteins myoglobin and hemoglobin fold?
Where about (wavelength range) do aromatic amino acids absorb in the UV-visible spectrum

WRT to protein structure - What is hemoglobin a good example of?

WRT to protein structure – What is plastocyanin a good example of?

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)

Be able to recognize the important rings – be able to draw PPIX – chlorophyll a
What does denaturation mean? How can it be observed? Is it reversible?

How does Mg^{2+} become involved in ATP etc.?
What is the structure of the polynucleotide chain?
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)

Know there is a major/minor groove - rise per turn (5.4 A)

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
Where does protein formation take place in the cell?

What is the structure of lipids – 3 types, sat/unsat/polyunsat (which is one your instructor should eat, NOT eat?)
Know that all sorts of chemistry take place through the membrane

Structure of prokaryotes vs eukaryote cells – which are typical of mammals?

Kingdom	When Evolved	Structure	Photosynthesis
Prokaryotes:-			
Bacteria	3 to 4 billion years ago	Unicellular	Sometimes
Archaea	3 to 4 billion years ago	Unicellular	No
Eukaryotes:-			
Protista	1.5 billion years ago	Unicellular	Sometimes
Fungi	1 billion years ago	Unicellular or Multicellular	No
Animalia	700 million years ago	Multicellular	No
Plantae	500 million years ago	Multicellular	Yes

First free oxygen in atmosphere
Banded iron (rust) formations appeared in inorganic geochemical record 1.8 BYA.
Soluble iron (II) oxide (FeO) was oxidized and precipitated out of ocean water as iron (III) oxide (Fe2O3)
Source was photosynthetic bacteria.

First eukaryotic cells
1.5 BYA
Shortly after increase in atmospheric O2 killed most anaerobic bacteria (e.g., tetanus).
First cells to have nucleus and organelles like mitochondria and chloroplasts.

Time line
4.5 BYA Earth formed
3.5 BYA First prokaryotic cell
1.5 BYA First eukaryotic cell
0.7 BYA Multicellular organisms
0.53 BYA Cambrian "Explosion"

Rise of Multicellular Organisms
Soft-bodied worms, jellyfish appeared 600-700 MYA, but most decomposed by bacteria before they could be fossilized.
Multicellular organisms (with hard body parts) become abundant at the start of the Cambrian period (about 543 MYA)
Diversity "exploded" 530-525 MYA.

Precambrian fossils
700-544 MYA
Multicellular, but soft bodied: worms, algae, jellyfish, cyanobacteria.
Few specimens preserved.
Probably much more abundant in life than in fossil record.

Cambrian Period
544 MYA First fossils of "hard bodied" organisms (shells, etc.) appear.
530-525 MYA An explosive "radiation" of life forms -- including all the animal phyla (major body plans) in existence today, plus many others now long extinct.

Fossils of the Burgess Shale
515 MYA a major underwater mud slide buried animals into deep, oxygen-free water and so preserved both hard- and soft-bodied diversity, even internal structures (guts)
These underwater layers now exposed in an outcropping in the Canadian Rockies.
Excavated in early 1900's, then ignored.

Ozone layer
450 MYA a ten-fold increase in atmospheric oxygen lead to increase in ozone formation (O2 --lightning--> O3)
Ozone provided protection from UV radiation which had previously been too intense for life to exist on land.

Terrestrial vertebrates
350 MYA fish "walked out of the water"
Probably not like present-day "walking catfish"

Age of the dinosaurs
200-65 MYA
Dinosaurs filled most of the niches occupied by present-day mammals: large and small herbivores and carnivores.
Mammals were present, but small-bodied and nocturnal.

And so on ….

QUESTIONS

What are vitamins? Define the term.
How they classified
What is the classification of the cobalt containing vitamin?

What is a coenzyme?
What is an apoenzyme?
Holoenzyme?
What is the effect of deficiency in vit B12?

We didn't cover cobalamin in detail this year 2018 so questions below for interest.

What is the oxidation state of the metal when bound to the axial group?
What does cobablamin catalyse ?
What is Homocysteine? What is methionine?
Why is folic acid connected with B12 activity?
Is there one form of B12?
Name 4 axial groups

FROM THE TERM TEST…

TOPIC: Zinc

Major points to review:

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

QUESTIONS

What are the common ligands for Zn in biological systems? The donor atoms? The amino acids? The molecules?
Name 5 different Zn-containing proteins or enzymes

What is Zn essential for in mammals?

What does deficiency result in?

Under what conditions is severe deficiency found in humans?
What is special about metallothionein?

What are the ligands in metallothionein?
What is the reaction catalysed by CA?
What are the ligands for Zn in CA?
What is the effect of pH on CA activity? Why is this the case?
What is the key reaction that Zn is involved with in CA?
What is a protease?
Why do we need them?
How is the Zn bound in CPA?
What is the key feature of this reaction? What makes it work?

What is the role of water in this reaction?
What do the hydrogen bonds do in CPA?
How many Zn are there in liver alcohol dehydrogenase? LADH

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

TOPIC: Toxic Metals

Major points to review: (note that the yellow highlighting identifies key points – the text around those key points amplifies and explains the heading)

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

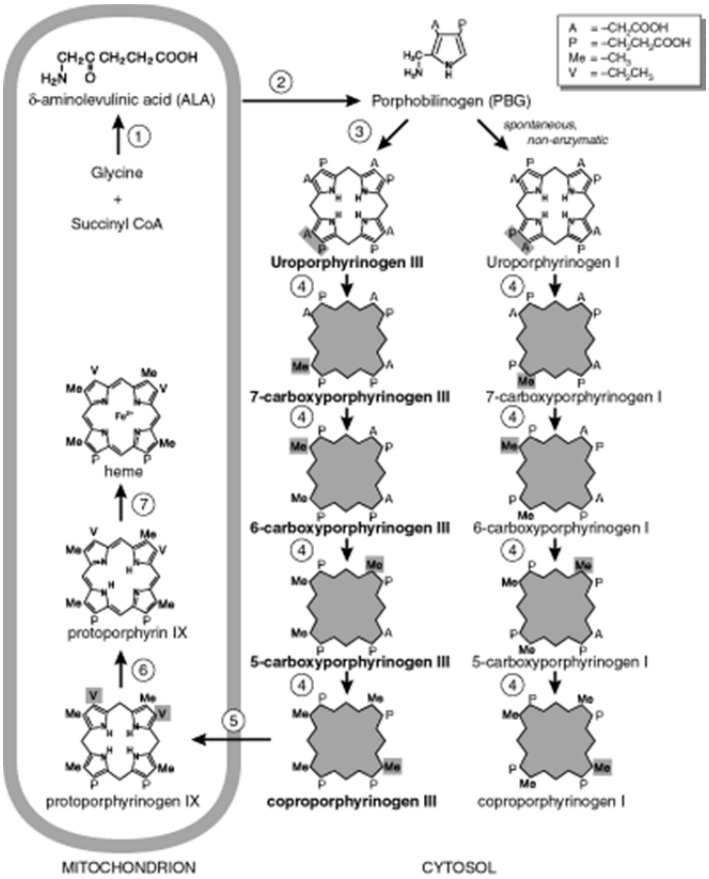
Toxicity depends on speciation – know what changes the speciation – know what increases solubility - very important to know the species that is most toxic
Know key metals
Know example of mercury – speciation – toxicity – where - when
Know cadmium, lead and arsenic
Mercury – cations vs methylated forms; Minamata Disease – what, why, where, when, where else
Cadmium – only cations – itai itai disease
Arsenic - - 3+ vs 5+; drinking water; protecting wood in the ground
Lead
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)
Know routes of exposure and toxic response – acute vs chronic
Poisoning in … - not included in the exam.
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.
Chelators – as before – now with metals connected – know top 2 chelators for each metal (Pb, Cd, As, Hg).
Where do toxic effects occur?

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

What are toxic metals?
Which metals are very toxic?
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?
What is the Bertrand diagram? What does it tell us?
What sort of diseases do toxic metals cause?
Is there any difference in the site of the toxicity for each metal or do they all cause the same sort of damage?
Which toxic metals commonly found around the home?

Why are many toxic metals classified as intermediate or soft?
What are the primary exposure routes for humans?
What does acute and chronic mean wrt to toxicity?
Why are the kidneys and liver prime sites for damage from most toxic metals?
What does LD50 mean?
About what quantity represents a super toxic material? What might this be?
How do metals enter the cell? Name 4 routes
Why is crossing the blood brain barrier so often referred to when speaking of mercury?
Why did the Romans have an issue with Pb?
How is heme synthesis related to the presence of Pb?
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
What does exposure to Pb result in for children?
Is Pb as deadly in adults?
How does Pb lead to anemia?
How has a change in gasoline been mirrored in the humans?
Where is Pb used in products?
Where is Pb likely an exposure risk to humans?
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



How is Pb measured in humans?

About what is the Pb exposure level that results in damage to children?

Why are ducks at risk from Pb poisoning?

How is mercury released into the environment?

How does mercury affect health of humans?

What are the conditions toxic metals become a concern?

What cases of poisoning by toxic metals are well known? Which metals?

Why do acidic fruit drinks pose a hazard?

How is cadmium different from mercury in its toxicity?

Why is cadmium a problem in the workforce?

Is cadmium a problem in the home?

Why is dental amalgam considered potentially dangerous?

What is the concern with some vaccine solutions?

Are there restrictions on the consumption of fish? Why?

Why is smoking so dangerous (other than nicotine and lung cancer)?

Why are computers a problem?

Where in the world is mercury a current problem?

Are there any elements/compounds that protect mammals from the effects of toxic metals? What are they?

What makes a metal toxic?

Is it easy to identify a toxic metal?

Which metals are absolutely toxic?

Which metals may be essential at some concentration?

Which metals are always non-toxic?

Which As compounds are not toxic?

A major recent concern from As poisoning has been the chemicals used for pressure-treating wood:

How are people exposed to arsenic?

Arsenic is the most common cause of acute heavy metal poisoning in adults

Why is pressure treated wood such a problem?

How significant is the health risk posed by CCA-treated wood?

CCA= chromate copper arsenate – dyed green

What are currently considered the best methods of making a CCA lumber surface safe from arsenic exposure?

How can I minimize arsenic exposure if my child plays on CCA lumber?

Can I use CCA-treated wood in fireplaces? In a wood-burning stove?

What precautions should I take when handling CCA wood?

What about arsenic contamination of the soil or sand under and around CCA wood structures?

What should I do if CCA wood is in or near my garden?

How long does CCA lumber continue to be an arsenic exposure hazard? Does risk go down over time?

Is there any way to look at CCA lumber surfaces and tell how much arsenic might come off from hand contact?

What was Lewisite? Where was it used? What is BAL?

What is the concern with As and water?

Where does the As come from in water?

How many people are affected? Roughly.

What are the major symptoms of chronic As poisoning?

What is glutathione? How does it bind to As?

Where in the world are the worst outbreaks of As poisoning today?

Is As a concern only there?

What causes the As to be released into the water?

What is the concern with Cd?
Does Cd poison like Hg?
Is Cd short lived in the body?
What is the major disease caused by Cd?
Where is Cd used in products?
What are the target organs for Cd damage?
Where does Cd enter the environment from? How are we exposed to Cd?
What is metallothionein's role in Cd metabolism?
What happened in Japan wrt Cd?
How many toxic forms of Hg are there?
Have there been instances of Hg poisoning world wide?
Why?
In Canada? Why?
What are the exposure routes for man?
Where is Hg used in products?
Where are we most usually exposed to Hg?
What are the health effects of Hg exposure? Are there differences depending on the form?
How does glutathione become involved with Hg?
Why is Hg^0 so dangerous?
Where is the target organ for methyl mercury?
Where are we exposed to methylmercury?
What detoxifying agent that could be used?
Where do fish and shellfish enter into the Hg story?
How? Why?
Is exposure the Hg fast acting or slow?
Can hair be used to assess Hg exposure?
What happened in Minamata? When? Where?
When was the case closed?

Critical questions to consider:

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?

All discharges of toxic metals are prohibited in Canada and have not occurred for the last 100 years since we understaood that some metals were toxic.

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?

Are there different effects depending on the dose of a toxic metal?

How dangerous is mercury?

Are we exposed to Hg routinely in our daily lives?

Are the fish safe to eat?

What is the problem with rivers in Ontario? Explain the origins of the Hg in rivers.

Why is this Hg so deadly? What happens next, how?

And, where in medicine do we become exposed to Hg?

How is heme synthesis related to the presence of Pb?

See above

Qu. 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

CHELATION THERAPY AND CHELATORS

What is chelation therapy?

How is it applied?

How does it work?

What makes a 'perfect' chelator?

What are the molecules used commonly today?

Can you draw their structures?

What is a common theme between the chelating molecules and the metals they chelate?

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Chelating Agent	Toxin	Route**	Drug
Dimercaprol (BAL)	Arsenic Lead Mercury (inorganic)*	i.m.	Dimercaptol Injection B.P. BAL in Oil
Dimercaptosiccinic acid (DMSA) (Succimer)	Arsenic Lead Mercury	p.o.	Chemet
Dimercaptopropane- sulfonate (DMPS)	Arsenic	p.o. i.m.	Bulk form (for compounding by pharmacists)

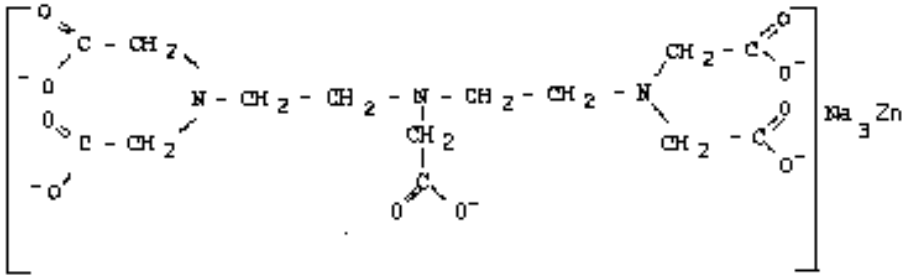
D-pencillamine	Arsenic Mercury Lead	p.o.	Metalcaptase Pencillamine Cuprimine Depen
Ethylenediamintetra- acetic acid (EDTA) (Edetate disodium)	Lead	IV	Chealamide Versenate

*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.

What about the biological chelators metallothionein? – See below for a follow up question.

Qu. Explain how this molecule might act as a chelators. Which metals would you predict it would bind. Why? What is is most like as a molecule?



QU: Discuss the reason for the following statements that concern the protein metallothionein – first –

- what is metallothionein?
- What is its role in the cell?
- What type of metal binding protein is it?
- What are the metal binding ligands?

High metallothionein may be indicator of heavy metal toxicity, especially for cadmium and mercury.

Low reduced glutathione is indicator of genetic diseases as well as indicator of exposure to toxic halogenated chemicals and heavy metals

Low reduced glutathione may decrease function of metallothionein

Qu. Consider the following statements. The assumption is that both Zn and Cu are absorbed from the diet – so what type of toxic effect is this going to be? What would you consider could be the role of metallothionein? What is your view – considering all the information?

The idea is that if MT is low, then metals cannot be removed as quickly as needed. This may lead to higher copper levels. So the idea is to get MT levels up to help bring copper (or other metals

or toxins) down. MT needs 7 molecules of zinc to 'activate' and capture some metals/toxins. If zinc is low, it is hard to get MT functioning well.
Let's say you start giving zinc which activates some MT. Let's say the MT grabs some copper. So when you supplement with too much zinc too fast, you fill up the MT you have. Well, the MT then leaves the body with the copper it grabbed along with the 7 molecules of zinc - or at least a chunk of them. So now you are deficient 7 zincs although you did get out some copper at the same time.

You give more zinc, more MT is made, takes more zincs, MT is activated, it grabs more copper and leaves the body taking the toxin and all the zincs along with it. The MT may not exclusively grab the zinc from the supplement you take. It might take some from the supplement source and the rest from other places in your body. If you were sort of deficient anyway and the MT is soaking up all the zinc, you become more deficient even though you supplement. The MT is soaking the zincs up even though it is also removing some of the copper or whatever toxin.

Mg and photosynthesis

Know the chlorophyll molecule
Know the structures of the key molecules along the chain
Know the oxidation numbers of the key accessory molecules PQ NADPH FD
Know the ribulose molecules and that cycle
Know the oxygen evolving complex molecule and its cycle
Be able to describe why PQ is so important to the electron
Be able to spell thylakoid correctly!! Lumen? Stroma?

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