

Jeopardy

MHD & Therapeutics

And Now Here

Is The Host . . .

FLIPPAARD

Insert Name Here

The categories for today's
Jeopardy on Sedative-
Hypnotics will be:

GABA-A or -B

Isoforms

Benzos

Non-Benzos

Miscellaneous

GABA-A or -B

GABA

Benzos

Non-Benzos

Miscellaneous

100

100

100

100

100

200

200

200

200

200

300

300

300

300

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400

400

400

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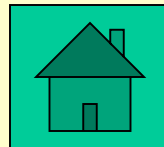
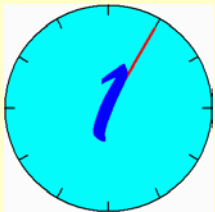
900

900



What is GABA-A?

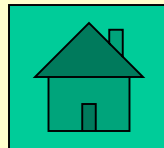
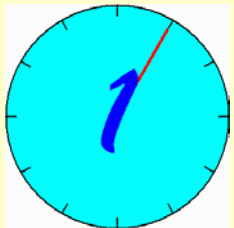
**Mucimol is an agonist and bicuculline
an antagonist of this receptor**



Row 1, Col 1

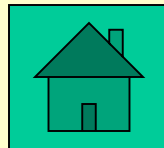
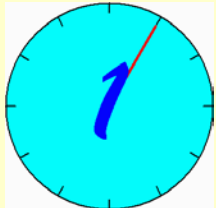
What is GABA-B?

**This receptor acts by causing a decrease
in Ca^{++} conductance**



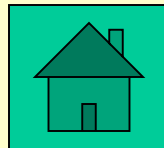
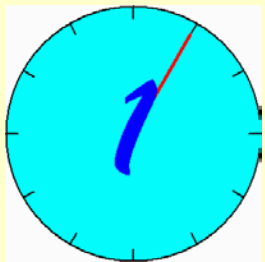
What is GABA-B?

**Baclofen (Lioresal) is a selective
agonist of this receptor**



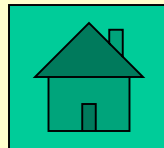
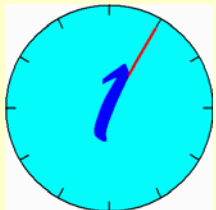
What is GABA-A?

**Benzodiazepines & other sedative
hypnotics modulate this receptor** 



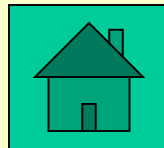
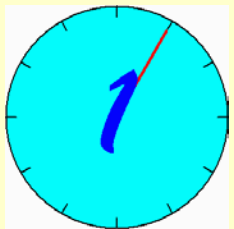
What is GABA-B?

This receptor acts by causing a hyperpolarization via an increase in K^+ conductance



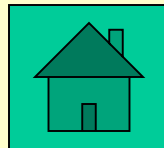
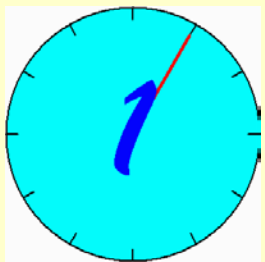
What is GABA-B?

**This is an metabotropic G-protein
linked receptor** 



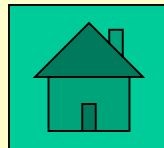
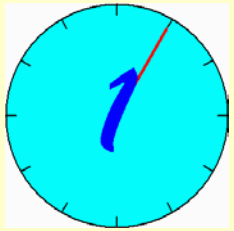
What is GABA-B?

**Benzodiazepines & other sedative
hypnotics do not modulate
this receptor**



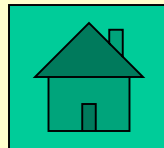
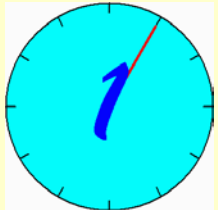
What is GABA-A?

This is an ionotropic receptor



What is GABA-A?

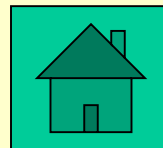
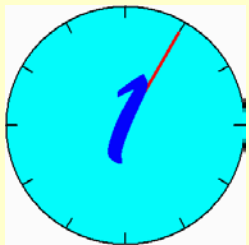
This receptor acts by causing an increase in the opening of Cl channels



What is α ?

α β γ ρ

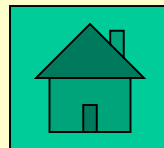
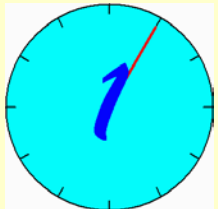
**There are 6 different isoforms of
this type of subunit**




2,1

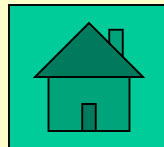
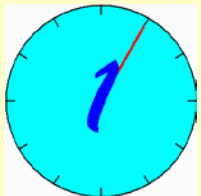
What is 5? (heteropentameric)

**The GABA-A is composed of
this many subunits**



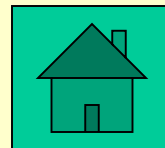
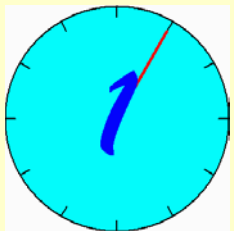
What is GABA?

Because the benzodiazepine receptor is an allosteric modulatory site, in addition to  the benzodiazepine, this needs to be present to alter the function of the GABA_A receptor



What is α - γ ?

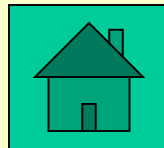
Previously referred to as the benzodiazepine receptor, this binding pocket is located at the interface of these subunits



2,4

What is α_1 ?

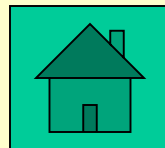
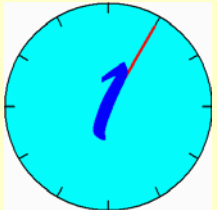
Regarding the benzodiazepine receptor, α_1 , α_2 , α_3 , α_5 isoforms all bind benzodiazepines, but only this isoform binds imidazopyridines & pyrrolopyrazine



What is α_4 & α_6 ?

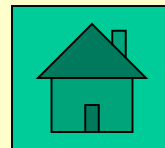
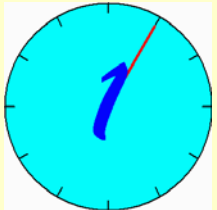
α_1 α_2 α_3 α_4 α_5 α_6

GABA receptors with these 2 α isoforms are diazepam insensitive



What is α - β ?

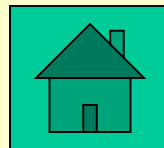
The region at the interface between these two subunits provides 2 sites for both GABA agonists and antagonists



2,7

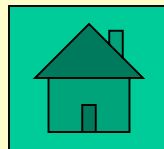
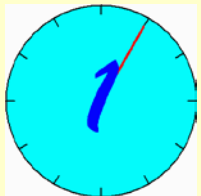
What is 2α , 2β , 1γ ?

While there are many possible combinations, the most common GABA-A receptor subtype is a generic composition of these subunits



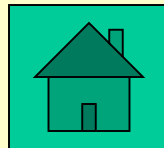
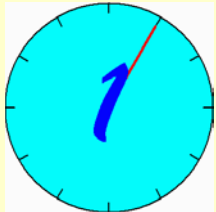
What is two sites?

While the α - γ interface provides a binding pocket for 1 benzodiazepine, the α - β interface provides this many site(s) for GABA agonists & antagonists



What is lorazepam, oxazepam, & temazepam?
(Ativan, Serax, & Restoril)

Benzos that have a short $t_{1/2}$, do not go through Phase I metabolism & are known by the mnemonic LOT are this, this, & this



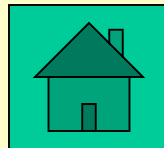
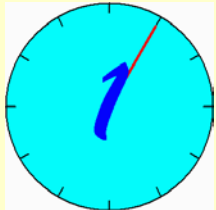
3,1

What is alprazolam (xanax)?

Alprazolam (Xanax)
Chlordiazepoxide (Librium)
Chlorazepate (Tranxene)
Diazepam (Valium)

=====

**All have desmethyldiazepam as a
bioactive intermediate except this**

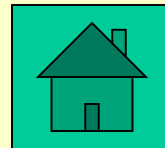
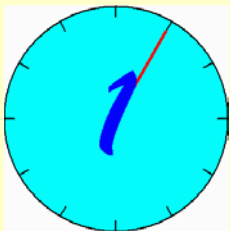


What is Midazolam (Versed)?

Alprazolam (Xanax)
Clonazepam (Klonopin)
Lorazepam (Ativan)
Midazolam (Versed)

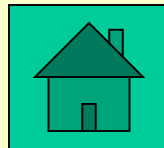


**Of all the benzos, the one primarily used IV
in anesthesia that has a very short $t_{1/2}$ &
a very fast onset of action is this**



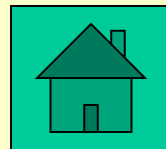
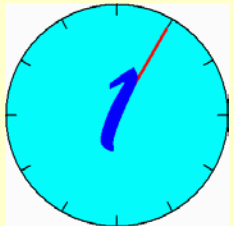
What is amnesia?

For victims of date rape who were given Flunitrazepam (Rohypnol®), this common benzo side effect hinders efforts to bring the criminal to justice



What is opioids?

The majority (80%) of benzo abuse is part of polydrug abuse by patients, most commonly with this drug



3,5

What is duration/half-life & time to action onset?

Duration/half-life

Time to action onset

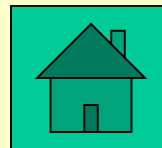
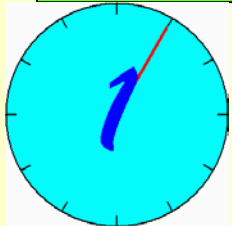
Time length drug taken

Potency

Dose

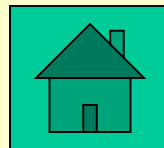
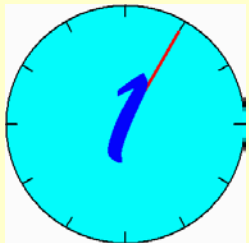


**Risk of developing tolerance increases as
this(these) factor(s) decrease**




What is drug accumulation?

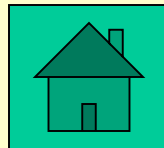
Benzos with long $t_{1/2}$ or bioactive metabolites should not be prescribed for daily use in elderly patients or patients with compromised liver function due to the risk of this



3,7

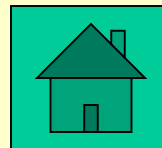
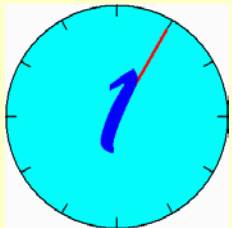
What is taper down the drug dose?

If discontinuing benzos on a patient at high risk of withdrawal, treatment strategies include switching to a longer $t_{1/2}$ benzo  (with lower potency and less rapid onset of action) and gradually doing this



What is **anxiolytic (or muscle relaxant) effects?**

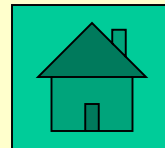
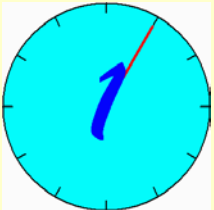
While tolerance may develop to the sedating effects of benzodiazepines, tolerance has not been observed to this effect



3,9

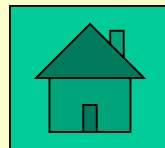
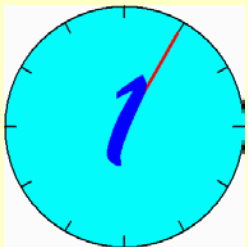
What is barbiturates?

**GABA is not needed for the GABA-A's
Chloride channel to open in the presence
of higher doses of drugs from this class**



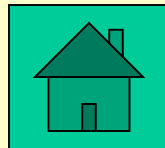
What is ramelteon (rozerum)?

Melatonin 1 & 2 receptors are bound, but benzodiazepine receptors are not, by this unique sedative hypnotic drug



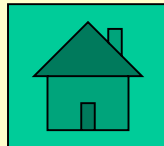
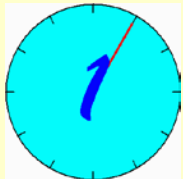
What is zaleplon (Sonata)?

A particularly short $t_{1/2}$ results in minimal morning after sedation for this selective non-benzodiazepine from the imidazopyradine class



What is eszopiclone (lunesta)?


**Being able to prescribe for longer term use
in the treatment of insomnia is an
advantage for this pyrrolopyrazine drug**

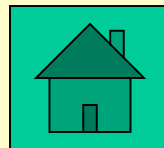
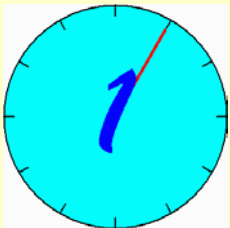


What are Barbiturates?


**Pyrrolopyrazine
Imidazopyridine**

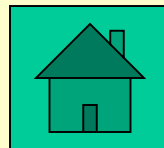
**Barbiturates
Benzodiazepine**

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Due to a low therapeutic index, risk of abuse,  dependence & withdrawal, & stimulation of P450 activity and hepatic microsomal oxidases, the most dangerous sedative hypnotic is this



What is zolpidem (Ambien), zaleplon (Sonata) & eszopiclone (Lunesta)?

Complex sleep related activities like  sleep driving and sleep eating may be a side effect with these 3 medications



4,6

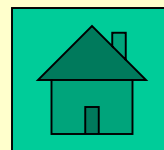
What is **Barbiturates** to **Benzos** to **Imidazopyridine** to **Pyrrolopyrazine**?

Pyrrolopyrazine
Imidazopyridine

Barbiturates
Benzodiazepine



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The order, from the highest risk of becoming habit forming to the lowest risk, is this

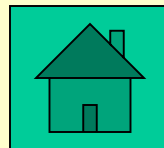
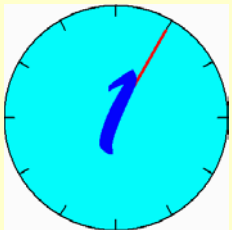


What is Benzos, Pyrrolopyrazine, & Imidazopyradine?

Pyrrolopyrazine Barbiturates
Imidazopyridine Benzodiazepine



**A competitive antagonist may be used to
treat patients who have overdosed on this
(these) med(s)**

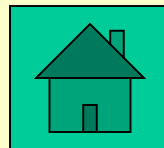
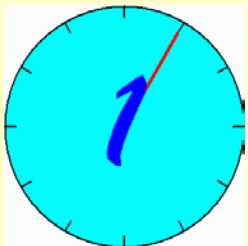


What is flumazenil (Romazicon)?

**Pyrrolopyrazine
Imidazopyridine**

**Barbiturates
Benzodiazepine**

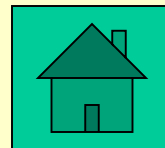
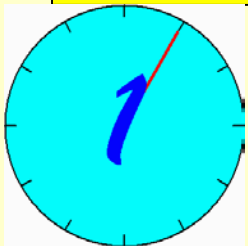
**The competitive antagonist that may be used
to treat patients who have overdosed on at
least 1 of these meds is this**



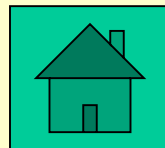
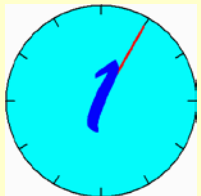
What is Clonazepam (Klonopin)?

Lorazepam (Ativan) 1 mg
Clonazepam (Klonopin) 0.25
Alprazolam (Xanax) 0.5 mg
Diazepam (Valium) 5 mg

**While equivalent doses, the most
potent drug is this**

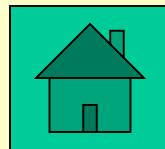


While diazepam (valium) does not have a short half life, it is highly lipophilic which increases the risk for this



What is **nothing**?

If an alcohol intoxicated patient is given flumazenil (Romazicon), this will happen




What is 4 & 6?

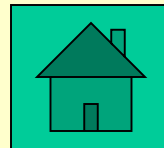
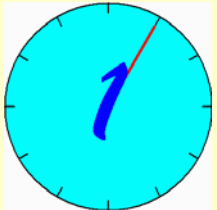
3

4

5

6

Lack of effects from a high dose of  diazepam (valium) is due to GABA receptors with this α isoform



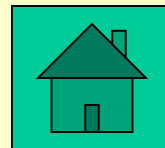
5,4

Chlordiazepoxide (Librium)
Diazepam (Valium)



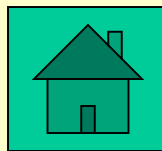
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**The parent compound that has a longer
half life than its common metabolite of
desmethyldiazepam is this**



What is flumazenil blocks zolpidem's effects ?

If a patient who has overdosed on zolpidem (Ambien) is given flumazenil (Romazicon), this will happen



5,6

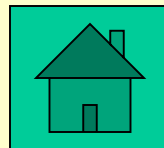
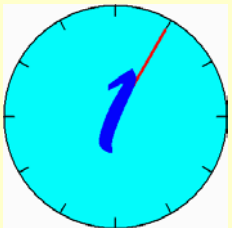
What is **Barbiturates, Benzos?**

Barbiturates-duration

Benzos-frequeuncy

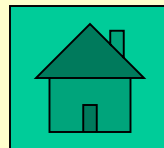
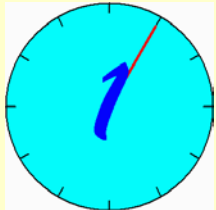
Benzos, Barbiturates
Barbiturates, Benzos

In the presence of GABA, the duration
the chloride channel is open is ↑ by
this, whereas the frequency of the Cl
channel opening is ↑ by that



What is sleep walking?

Benzodiazepines—at least in theory—could be used to treat this sleep related side effect of both zolpidem (Ambien) & zaleplon (Sonata)



What is cleft lip/cleft palate?

While different studies do not agree, use of benzodiazepines during pregnancy may increase the risk of this teratogenic outcome

