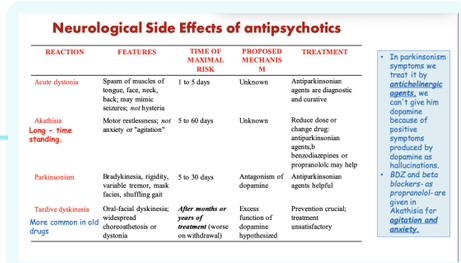
Schizophrenia

features
- pathogenesis is unknown
  - a thought disorder
- onset
  - is in the late teens-early '20s
  - affects 1% of the population worldwide
- genetic predisposition
  - familial incidence
  - hereditary influences may account for 10% of schizophrenia cases
  - multiple genes are involved
    - doesnt mean that the genes decide whether you are schizophrenic patient or not
    - so there is no specific genes that affeects it but many genes increase the persons risk
- more of a male disorder more than females and they differ in onset
  - females
    - after 28, every 200
  - males
    - starts teens, early 20s, every 100
  - the cause of onset differenes is due to
    - environment
    - genetic makeup
- the drugs that we use are for the prevention of psychosis so keep in mind that these drugs ARE NOT A CURE
  - schizophrenics must be treated with medications indefinetly in as much as the disease in lifelong and it is perferable to prevent the pyshcotic episodes than to treat them
    - schizophrenia is for life
    - there is no remission
- dopamine theory of shcizophrenia
  - many lines of evidence point to the aberrant increased activity of the dopaminergic system as being critical in the symptomatolgy of schizophrenia
  - there is a greate occupancy of D2 receptors by dopamine--> greater dopaminergic stimulation
- schizophrenia pathophysiology and pharamcologic profile of APDs
  - schizophrenia pathophysiology
    - past
      - excessive dopamingergic activity
    - present
      - renewed interest in the role of serotonin (5-HT)
  - pharmacologic profile of APDs
    - past
      - dopamine antagonist
        - D2 receptors
        - this is the typical drugs site
    - present
      - combine antagonists
        - 5-HT2/D2
        - atypical drug sites
  - In the past they used to think that the problem is only with the excess dopaminergic activity. But they discovered that the serotonin receptors (5-HT) also have a role in this disease, how did they know? They saw that the patient is over-excited (hallucinating), cannot get things together, the cognition is inhibited (he can't make a single meaningful sentence) & at the same time he's depressed. They said that if we inhibited the serotonin receptors (5-HT) this will cause mood improvement. & from here they discovered the ATYPICAL antipsychotics which inhibit DA receptors & serotonin receptors
- neurological side effects of antiphysotics
  - in parkinsonims symtoms we treat ut by anticholinergic agents, we cant give him dopamine beccause of positive symtpoms produced by doapmine liek hallucinations
  - BDZ and beta blockers like propanolol are gven in akathisia for agitation and anxiety
  - Schizophrenia is Alife- disease, the drug will be taken for ever to control the symptoms, these includes that we open the mind of the patient, and his thoughts cross over each other. the doctor isn't not interested by those effects, just to know the patient are tolerated the drugs until sedition state
  - 

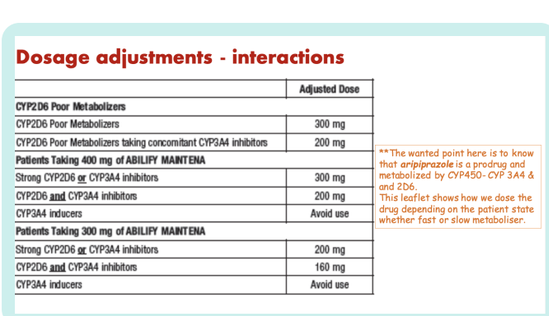
- tolerance and dependence to antiphsycotic drugs
  - not addicting
  - relapse in physcosis if discontinued abruptly
  - tolerance develops to sedative effects
  - no tolerance to antipsychotic effects because this is an antagonist effect
- withdrawl like syndrome
  - symptoms
    - nause
    - vomitting
    - insomnia
    - headache
    - sedation
  - these symptoms may persist for up to 2 weeks
  - these symptoms can be minimized with a tapered reduction of drug dosage

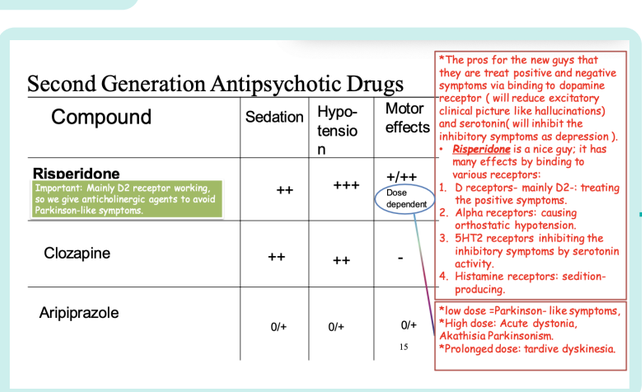
symptoms
- positive symptoms
  - hallucinations
    - delusions (bizarre, persecutory)
    - disorganized thought
    - perception disturbances
    - inappropriate emotions
- cognition
  - new learning
  - memory
- negative symptoms
  - blunted emotions
  - anhedonia
  - lack of feeling
- mood symptoms
  - loss of motivation
  - social withdrawl
  - insight
  - demoralization
  - suicide

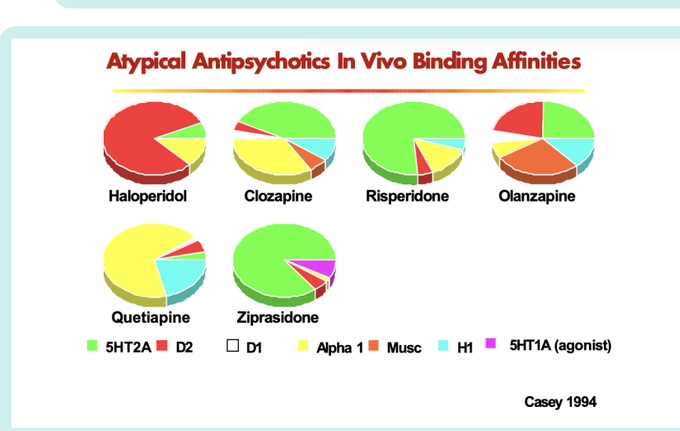
Main Topic 4

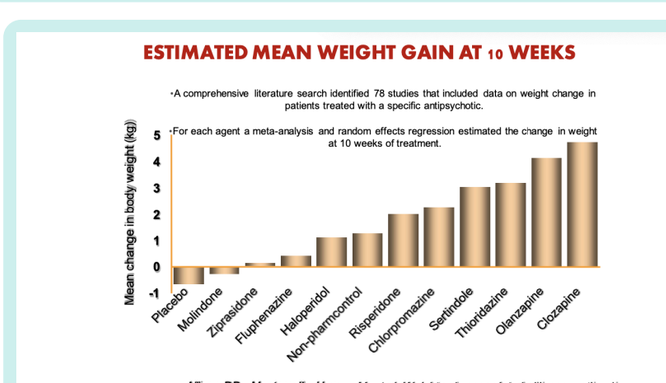
Drugs
- Postivie symtpom drugs
  - Haloperidol
  - Fluphenazine
  - MOA
    - affects the dopaminergic receptor, mainly D2 in which theyjust decrease the positive symptoms like hallucinations
  - features
    - so we also need to use a drug that reduces the negative symtposm too
- Negative symptom drugs
  - Clozapine
  - Olanzapine
  - Risperidone
  - MOA
    - bind to depoamine and serotonin receptors
  - features
    - less likely to make mentiones side effects because of unselectivity - which means they arent selective towards dopamine since they bind to serotonin too
- classification of antipsychotics
  - typical antipsychotics - old
    - phenothiazines
      - cholopromazine
      - perphenazine
      - fluphenazine
    - thioxanthenes
      - flupenthixol
      - clopenthixol
    - butyrophenones
      - haloperidol
      - droperidol
    - First Generation Antipsychotic Drugs

Compound	Seda-tion	Hypo-tension	Motor (EP) Effects
Phenothiazines			
Chlorpromazine	+++	++	++
Fluphenazine	+	+	++++
Haloperidol	+	+	++++

  - atypical antipsychotics - new
    - clozapine and olanzapine
      - features
        - clozapine is the best drug among them all
        - olanzapine has low affinity so less side effects
        - they have very low EPS- extrapyramidal symptoms
        - may show greater efficacy against negative symptoms than other antipyschotics
      - MOA
        - blocks receptors
          - D1
          - D2
          - D4
          - adrenergic
          - 5HT2
          - muscarinic
          - histamine H1
            - sedation effect
      - side effects
        - agranulocytosis
          - potential fatal side effect for clozapine
          - thats why we should always check for the blood count
        - both drugs have a high efficacy but cause significant weight gain and diabetes
          - the diabetes condition caused by blocking 5HT2 C receptor, so we block the axis between serotonin and insulin as well as disrupt the relation between them .
    - risperidone
      - features
        - one of the most perscribed drugs in Jordan
      - MOA
        - mainly D2 receptos working, so we give anticholingergic agents to avoid parkinson like symptoms
          - so they decrease the dopamine but the prolactin will increase
        - binds to many receptors like
          - D receptors - mainly D2
            - treating the positive symptoms
          - Alpha receptors
            - causing orthostatic hypotension
          - 5HT2 receptors
            - inhibiting the inhibitory symptoms by serotonin activity
          - Histamine receptors
            - sedation producing
      - side effects
        - in women
          - galactorrhea
          - loss of libido
          - delayed ovulation and menstruation or amenorrhea
        - in men
          - gynecomastia
          - importence
        - Risperidone has the most notable endocrine effects as result of dopamine receptors inhibition mainly
    - sulpiride
    - quetiapine
      - features
        - no increased risk for extrapyramidal symptoms
        - DOES NOTTT elevate prolactin
      - side effects
        - shares sedation
        - orthostatic hypotension
        - weight gain
        - anticholinergic side effects
          - dry mouth
          - constipation
    - ziprasidone
      - features
        - smilar advantages of others, but argued NOT to case wight gain
        - Clozapine – 1.7 kg/month; Risperidone – 1 kg/month; Olanzipine – 2.3 kg/month; Ziprasidone – 0.8; Quetiapine - 1.8 kg/month
    - arpiprazole
      - features
        - japanese product
        - few extrapyramidal side effects
        - its a prodrug
        - metabolized by CYP450 - CYP3A4 and CYP2D6
          - 

      - MOA
        - parital agonist at D2 receptors
          - due to minimal effects on the receptors as a partial agonist, It gives good outcomes on the long-run treatment, avoiding the abovementioned side effects
        - has an affinity to many receptors
          - muscarinic
          - alpha 1 adrenergic
          - serotonin
          - histamine
      - side effects
        - weight gain
        - feeling dizzy
    - 

      - the advantage of these new drugs is that they treat both the positive and negative symtpoms
        - positive symptoms
          - binding to dopamine receptors
        - negative symptoms
          - binding to serotonin
    - 

    - 

  - the distinction between the typical and atupical groups isnt clearly defined but rests on
    - incidence of extrapyramidal side effects
      - less in atypical group
      - the new guys make them by little onset
    - efficay in treatment resistant group of patients
    - efficacy against negative symptoms via afffecting the serotonin receptors